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A MONOGRAPH ON TREMBLES OR MILKSICKNESS AND WHITE SNAKEROOT

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AND B. F. KAUPP

NORTH CAROLINA
AGRICULTURAL EXPERIMENT STATION
CONDUCTED JOINTLY BY THE
STATE DEPARTMENT OF AGRICULTURE
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NORTH CAROLINA STATE COLLEGE OF
AGRICULTURE AND ENGINEERING

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A MONOGRAPH ON TREMBLES, OR MILKSICKNESS, AND WHITE SNAKEROOT.*

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INTRODUCTION

For a number of years, complaints have come to this Station through letters from farmers, county agents, and extension workers, of the occurrence within the mountainous sections of North Carolina of a peculiar malady known as Trembles. This disease annually causes very considerable losses of horses, cattle, sheep, and hogs. Furthermore, in sections where this disorder is present, the belief is unanimously and firmly held that man may contract the disease by the ingestion of milk, hence the name "milksickness" which physicians employ, of certain milk products and of flesh of animals affected with trembles.

A questionnaire was therefore sent out to learn, among other things, something of the distribution of trembles, the seasonal incidence of the disease, the kinds of animals affected, preventive and curative measures employed, losses, and opinions as to the cause. It was found from these reports that the disease very probably occurs in the mountainous portions of all the counties in western North Carolina and in the immediately adjacent sections of States having similar conditions. The losses, furthermore, to the live-stock interests are so grave, since the danger of an outbreak is ever present and since so few affected animals recover, except when cases are discovered and treated in the incipient stages, that the farmer is reluctant to make any considerable investment in stock in sections where the malady is likely to occur.

Not only is an additional risk placed upon live-stock production by the presence of this disease, but it also discourages certain industries such as creameries and cheese factories whose success depends upon a lively interest in the growing of domestic animals. The popular attitude toward the disease is typified by the report of one county agent, who asserts that in his section trembles is the limiting factor in the establishment of cheese factories.

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Numerous beliefs, too, many of which are shrouded in mystery, were found to be entertained in regard to the causation of the disease. An examination of the voluminous literature on trembles and milksickness revealed the fact that many of these beliefs had been expressed in print, and that even critical investigations dealing with the etiology of the malady contained diverse conclusions. The one apparently most widely accepted by investigators, however, is that the disease is of bacterial origin. This opinion is contained in a recent bacteriological text-book* which states that the disease "is caused by the growth of and consequent absorption of toxic principles from the infective agent (*Bacillus lactimorbi*) lodged primarily in the small intestine and, secondarily, in the liver and other organs of the body."

In view, therefore, of the immense economic importance of trembles and milksickness and of the conflicting statements in regard to its etiology, a study of the disease was begun in the summer of 1916. This work was continued throughout the succeeding year and a considerable body of data has been secured bearing on the cause, transmission, symptoms, and pathological anatomy of the disease. A preliminary report on the cause of trembles has been published,† but since the subject-matter of this report is included in the present paper, further mention of it is deferred at this place. It is deemed advisable, furthermore, since the readers of this bulletin may not have ready access to published accounts of milksickness, and consequently may not be familiar with the literature bearing on the disease, to include a considerable body of historical information.

HISTORICAL ACCOUNT OF THE OCCURRENCE OF TREMBLES AND MILKSICKNESS

This disease has for a long time been known to occur within the United States. Attention was first directed to its presence by a physician, Dr. Daniel Drake, who published, in 1810, a brief account of it under the title "New Disease" in his Notices Concerning Cincinnati. This account, which was communicated to Dr. Drake, was based upon observations made in Madriver County, Ohio, by Dr. Barbee. Drake's account consisted of a concise statement of the symptoms, kinds of animals affected, conditions favoring its prevalence, and remedial and palliative measures. This account was later reprinted by Drake as an editorial addition to an article by McCall (1830). While this note in 1810 is the first published account, the disease is known with cer-

Vide, Marshall, Charles E., edit. *Microbiology*, a text-book of micro-organisms, general and applied. 2d edition, p. 785, 1917.

†Journal of Agricultural Research. June, 1917.

tainty to have existed prior to that time. Drake (1836) makes the statement "that this malady has been observed in some parts of North Carolina more than sixty years ago (*i. e.,* prior to 1776) and that it had been an endemic in certain localities of Tennessee, Kentucky, and Ohio from their first settlement." Coleman (1822) states that "sick stomach has been prevalent in some of the western counties of the State of Ohio since their first settlement." McCall (1823) makes specific mention of several cases which occurred in North Carolina between 1779 and 1800.

Rawlings (1874) also makes reference to "its first avowed recognition in the State of North Carolina—now over ninety-six years ago" (*i. e.,* prior to 1778). It is further stated in this account that "the disease followed emigration in its westward march from North Carolina to Tennessee and Kentucky, and prevailed in various parts of Ohio, Indiana, and Illinois. The report of Carney (1847) mentions the occurrence of the disease, "I think sixty or seventy years ago (1777 or 1787) in the Carolinas" and "upwards of fifty years since, it prevailed in Kentucky." In speaking of the disease in Tennessee, Lea (1821) asserts that "as soon as settlements commenced in the county of Franklin, about 12 or 15 years since, near the mountain, many cattle were lost from some unknown poison, the nature of which is still a mystery among the inhabitants. Occasionally whole herds have been found dead in some sequestered cove of the mountains." There are also early records of the disease in Indiana made by Faux (1823) and in northwestern Missouri by Long (1823).

An interesting historical account comes from the pen of Flagg (1836) from observations made while he was in Monroe County, Illinois. This states that "a mysterious disease called the *milk sickness*—because it was supposed to be communicated by that liquid—was once alarmingly prevalent in certain isolated districts of Illinois. Whole villages were depopulated; and though the mystery was often and thoroughly investigated, the cause of the disease was never discovered. By some it was ascribed to the milk or to the flesh of cows feeding upon a certain unknown poisonous plant found only in certain districts, by others to certain springs of water, or to the exhalations of certain marshes. The mystery attending its operations and its terrible fatality at one period created a panic in the settlers; nor was this at all wonderful. The disease appears now to be vanishing."

Other writers share this idea that the malady is disappearing since Winans (1840) states that "I had three to five hundred patients during the whole time the disease prevailed. It has now nearly or quite vanished away." Beach (1883) in speaking of the disease in Madison

County, Ohio, "presumes nearly one-fourth of the pioneers and early settlers died of this disease." Compton (1881) in discussing conditions in Dubois County, Indiana, in 1815, says that "more than half the deaths that occurred in that section were from milksickness. It was also very fatal among stock."

While these opinions represent the belief of a considerable number who have known this disease, it is by no means universally shared. Among those who have expressed themselves differently may be cited Smith (1874) of Kenton, Ohio, who states in a letter to a medical journal, "We are having, this fall, a regular epidemic of what is generally called milksickness or trembles. I have treated upwards of thirty cases." In an article by Gray (1881) twelve cases of so-called gastritis developed among the consumers of butter from a certain farm. Three of these came under his observation and were apparently genuine cases of milksickness. Shapard (1892), of Winchester, Tenn., believed that the disease was as prevalent as at any time within the past fifty years. As recently as 1907, McCoy (1907) investigated an epidemic which resulted in six deaths in Macon County, Tenn. A recent report by Selby (1917) from the Ohio Station records the death from trembles of a cow at Sharpsburg, Ohio, in 1912, and of two at Johnstown, Ohio, in 1915. A communication was furthermore received at the Ohio Station in 1916 concerning the death of a young woman near Cygnet, Ohio, from milksickness.

Examinations of records of this disease in the various medical journals indicate that milksickness was more prevalent during the first half of the nineteenth century than during the latter half. This is to be expected since the lands in which white snakeroot (Eupatorium urticaefolium) grows have gradually been cleared and brought under cultivation. Even those who did not recognize this weed as the etiological factor in the production of this malady unanimously agree in the observation that thorough clearing and cultivation of the land will transform a dangerous area into a safe one (Drake, 1849; Crook, 1897; Pickard, 1857; Way, 1893).

Several reasons may be brought forward to show that the relative prevalence of this disease in times past cannot now be determined with any degree of exactness. In the first place, the International Classification of Diseases and Causes of Death does not recognize the existence of milksickness. This is not surprising, when attention is directed to the fact that at the time when the disease was most prevalent some writers, who expressed themselves voluminously on milk sickness, were very skeptical as to the existence of any such disease. Among these are Yandell (1852), who in criticising the various publications dealing

with the cause of the disease, gives it as his opinion that "the various accounts of this disorder nullify each other; and the mind is left in extreme doubt whether there is anything specific in milksickness." In discussing the existence of milksickness, Anderson (1867) has asserted that it is "a mere matter of credulous fancy." Other writers, as Chapman (McCall, 1823), Thompson (1854), and Bowen (Bailey, 1888) only go so far as to declare their disbelief in its existence.

A second reason for failure to determine the relative prevalence of this disease formerly is that health authorities have refused to record deaths reported under the name of milksickness. Again, genuine cases of milksickness have no doubt been diagnosed as gastritis, typhoid fever, ptomain poisoning, etc. This is to be expected since physicians have not had occasion to observe the malady while receiving their medical training, and so do not always identify it in practice.

THE CAUSE OF TREMBLES AND MILKSICKNESS.

The etiology of this disorder has been the subject of considerable speculation and investigation, but no one appears to have presented any convincing body of data in support of his conclusions. The solution of this question was regarded as of so much importance in the early part of the past century that rewards were offered by several State legislatures for the discovery of the cause. Even as late as 1904, Osler (1904) in addressing medical officers of the United States Army calls attention to this as one of the intricate unsolved problems.

Numerous articles have been written on the causation of this disease. In a general way, these can be classified as supporting one of the three following theories: (a) mineral poison theory, (b) germ theory, and (c) poisonous plant theory. One finds advocates also of other more or less plausible hypotheses some of which are mentioned later in this report. It is believed that the writers' evidence can best be presented after brief consideration has been given to some of the more important published accounts on this phase of the problem.

a. Mineral Poison Theory.

A number of observers, among whom are Shelton (1836) in Alabama, White (1836) in Indiana, and McAnelly (1836) in Kentucky, held that animals while grazing obtained some poisonous mineral which was present in the soil in affected regions. The last of these men believed also that this poison was present in well water and accounted for the occurrence of the disease in autumn by the lowering of the water table resulting in the poison becoming "more concentrated."

Among the minerals held to be the cause of milksickness are arsenic, copper, mercury, cobalt, lead, and aluminium. Seaton (1842) was a very vigorous supporter of the view that arsenic was the cause of the disease. His arguments were as vigorously opposed by Drake (1842) and by Yandell (1852).

McCoy (1907) failed to produce in guinea pigs any condition remotely resembling trembles in feeding experiments in which cobalt, lead, and arsenic were employed.

Moseley (1909) from feeding experiments with rabbits came to the conclusion that trembles was due to aluminium phosphate and that animals get this substance by eating white snakeroot. Proof of this claim consisted in feeding aluminium, which was present in the ash of white snakeroot and in the milk and butter of affected cows, and in developing trembles by the feeding of aluminium phosphate. He found this substance also in the ash of Bigelovia (rayless goldenrod) sent from New Mexico, where ranchmen claimed that it caused trembles among their cattle. In his experiments similar effects followed the feeding of rayless goldenrod, white snakeroot, and aluminium phosphate. Another paper published by Moseley (1910) about a year later affirms that soda exerts an antidotal effect upon aluminium phosphate.

One of the most potent reasons urged that the disease is associated with the soil itself, is a fact quite universally agreed upon by all observers. Cattle pastured upon particular tracts of land acquire milksickness, whereas others on adjoining pastures never show any sign of the disease. These milksick areas are believed to be so sharply delimited that farmers have fenced off areas to prevent the access of stock. In some places the changing of the fence so as to include even a few yards of uncleared land is held to be responsible for an outbreak of trembles. In White County, Tenn., McCoy (1907) states that the disease has been very rare in the locality of Milksick Mountain since it was fenced about sixty years ago. These enclosed areas sometimes occupy only a few square rods. Shelton (1836) records the fact that "in Blount County, Tenn., there is a locality embracing not more than ten or fifteen acres on which the disease has been known to originate for nearly, perhaps quite, forty years."

Wooded land has been held by a considerable number of observers to be essential for the existence of the disease. Drake (1841) from observations made in Ohio says "trembles in cattle, horses, sheep, and hogs are produced by their frequenting the densely timbered table land which from its flatness abounds in wet places and ponds, indicated by the presence of lofty white elms, black walnuts, maples, burr oaks, and other trees which delight in a rich moist soil." It is furthermore claimed

by Lea (1821) and Beach (1884) that cattle may contract trembles if left overnight in such areas, but if they are removed before dark the disease can be avoided. When such wooded land has been cleared, it is rendered harmless. Crook (1857) claims that "in no instance has it ever been known in this county (Spencer County, Ind.) during any other than the grazing season, and then *only* upon lands that had never been in cultivation." This is in agreement with the claims made by Bennett (1822), Pickard (1857), and Simon (1888).

Attempts have been made, also, to associate the disease with certain soil types. Seaton (1841) claimed that it occurred only where sandstone entered largely into the composition of the soil. Those who did not agree with this view based their opinion upon the wide geographical distribution of milksickness with the consequent wide variety of geological peculiarities.

Another observer, Allen (1878), who believed that the disease is closely associated with the soil, records the peculiar instance that in certain localities in Effingham County, Ill., cattle lick large holes in the earth, after which many of them die.

In a considerable number of instances, water from infected areas has been held to be responsible for the disease. White, as early as 1836, mentions instances of outbreaks among cattle and sheep attributed to water. Beach (1883) gives an account of trembles in cattle contracted after having eaten hay from a meadow which had been flooded by surface drainage from a tract of land notorious for producing the disease. More recently Lyday (1896) maintains that in North Carolina the drinking of water from streams that flow from milksick coves is responsible for the disease. Fulton (1884) cites an instance in Logan County, Ohio, where cattle had taken the disease until a certain spring was fenced off, whereupon there was no more trouble. Credible informants told him of the disease in cattle accustomed to be watered at a certain well in Clark County, Ohio. When the well was closed, the disorder disappeared. He also recounts an instance of "a farm in Hardin County on which members of every family that has ever lived there have had the disease. On that farm I have attended patients who said they had not used meat, milk, butter, or cheese for weeks, guarding against the disease. The presumption, therefore, was that they and also those of previous families that had lived there had obtained it directly from the water."

Others have considered water responsible for the transmission, and thus indirectly allign themselves with the germ theory to be next discussed. McAnelly (1836) states in support of water as the agency of transmission, that "the disease sometimes prevails in the human spe-

cies in districts where the inferior animals are comparatively exempt and frequently where none of them are known to be affected at that time." The following singular statements by Brewington (1876) express belief in the same idea: "I do not believe that in this vicinity there is one in fifty persons that take the disease who gets it by using milk or butter from diseased animals. In many places where the disease used to be most prevalent, the people used water from wells for cooking and drinking, but since they built cisterns and use water from them exclusively, they are entirely exempt from the disease."

b. Microbic Theory

Several early students of milksickness doubted the validity of the mineral poison theory as an explanation of the causation of the disease and manifested a belief in the microbe theory. They did not have the advantages, however, of modern bacteriological technic and, basing their judgment largely on the transmissibility of the disease, concluded that it must be caused by some microscopic organism. Both Wright (1827) and Reed (1856) felt that the failure of chemical studies to show the presence of a mineral poison and of botanical studies to inculpate any poisonous plant indicated that the cause must be sought among cryptogamic parasites.

Because of the transmission of the disease through meat and milk, Burger (1825) compared milksickness with anthrax. Heeringen in 1843, twelve years before the discovery of the anthrax bacillus, and Heusinger in 1853 also pointed out certain points of similarity between milksickness and anthrax. Wood (1858) on purely *a priori* grounds argued causation by a germ. The passage of the disease from one body to another and "its multiplication in the system" inclined Byford (1855) and DeBruler (1858) to the germ theory. Philips (1877) found "a great number of living, moving, spiral bacteria" in the freshly drawn blood and in the urine of a typical case. Woodfin (1878), too, believed that milksickness is a specific infection. Gardner (1880) reported finding "countless multitudes of actively moving, writhing, twisting bacteria" in the blood of a heifer suffering from trembles and in dogs affected by eating the flesh of this heifer. He furthermore found the same organism in the blood of two human patients, in the water of a spring which supplied this stricken family, and in milk. Microscopic examinations of blood by Schmidt (1877) failed to reveal the presence of bacteria.

Logan (1881) committed himself to the statement that the disease must be due to a "contagium vivum."

It is a common belief in some sections of the State that cattle exposed at night in "milksick areas" contract the disease. This has suggested conveyance of the infection through the bites of arthropods or certain insects.

A considerable number of writers who have studied the disease more recently than the ones just reported accept the theory of a parasitic origin of the disease. Among them are Maurel (1884), Boggs (1907), McCoy (1907), Crawford (1908), Jordan and Harris (1908, 1909), and Luckhardt (1909). The three last named authors alone have reported studies upon a definite microscopic organism. Jordan and Harris (1908, 1909), in their two extensive accounts, record the finding of an undescribed spore-forming bacterium, which they designate as Bacillus lactimorbi, in the liver, bile, and spleen of a heifer, in the liver of her fetal calf, in the pericardial fluid and gut nodule of a horse, in the brain, heart blood, and liver of lambs, in the feces of nonfatal cases in man, in the milk of cows, in the soil of milksick regions and in regions where milksickness has never been known, in normal cow dung, and on various grain and forage plants. They succeeded in several instances in isolating B. lactimorbi in pure culture from the heart blood and from certain internal organs of animals examined a few hours after death. They used in their experimental work rabbits, guinea pigs, dogs, cats, lambs, and calves. It may be briefly stated with reference to this work, that no well marked cases resulting in death were developed, although certain symptoms and lesions similar to those in animals naturally affected with milksickness were produced. In concluding their report, they assert that "taken as a whole, the facts do not indicate that a specific microorganism is the cause of milksickness or trembles. The bacillus in question belongs to a group which seems widely distributed and for the most part certainly not endowed with pathogenic qualities."

Luckhardt (1909) made further studies in the laboratories of Drs. Jordan and Harris on the physiology of Bacillus lactimorbi, on its distribution, and on its pathogenicity. He isolated the organism from alfalfa from farms in Wisconsin, Illinois, and Indiana, which supplied certified milk to Chicago and Milwaukee, and from four species of weeds, Bigelovia Rusbyi, Solanum elæagnifolium, Gutierrizia sphærocephala and Portulaca pilosa from the Pecos Valley, New Mexico. He furthermore isolated it twice from Roquefort cheese. Dogs were used in inoculation experiments. In discussing the results of this work the author concludes that "the preceding experiments are far from being decisive in establishing B. lactimorbi as the etiological factor in the production of milksickness. The organism either loses its pathogenicity very rapidly when grown on artificial media, or the virulence of the

organism is dependent upon what may be termed a symbiotic life or existence on certain plants. . . . On the other hand, it is remarkable that if B. lactimorbi be the cause of milksickness, it should have so wide a distribution in milksick and nonmilksick regions."

In a few cases certain molds and mushrooms have been claimed to be etiological factors. Among those who suggest that mushrooms are the poisonous agent are Winans (1840), Johnson (1866), and Gardner (1880). Hessler (1905) reports the finding of Sterigmatocystis, one of the cosmopolitan molds, in the blood of an affected heifer. Slack (1854) compared milksickness to ergot poisoning and believed the cause to be a "fungus production" on grass or grass seeds, a view also held by Nagle (1859).

Several other more or less fanciful causes of milksickness which cannot be classified under either of the three groups of causes have advocates within North Carolina and will, therefore, be briefly treated before giving consideration to the poisonous plant theory. Walker (1886) experimentally exposed corn fodder to the dew in a milksick cove and thus communicated trembles to a yearling. Farmers in some sections of North Carolina have come to believe that cattle which are penned up at night and not permitted to graze before the dew has evaporated are not liable to contract the disease. This same opinion has been expressed in the writings of Evans (1860), Reagan (1884), and Walker (1886). The influence of dew is only an apparent one as explained, in part at least, by Woodfin (1878), who says that cattle which are confined at night cannot range sufficiently far to reach the affected and usually remote tracts of land. The influence of dew is explained by Davis (1881) on the ground that animals eat more greedily of plants wet with dew than when they are dry.

A number of writers have adhered to the idea that the disease is produced by a gas or miasm rising from the earth. Lea (1821), Horne (1846), Jones (1862), and Wozencraft (1873) employ such terms as "an exhalation from the soil" and "peculiar miasma" in accounting for the disorder.

The claim has furthermore been made by Lescher (1850), Thompson (1853), Rawlings (1874), Dorsey (1876), and Sale (1871) that the disease resembles, in some respects, malaria.

Two accounts, Kennedy (1878) and Achelor (1884), which have come to hand, attribute the disease to the bites of a certain fly, an idea which would liken milksickness to the tsetse-fly disease or sleeping sickness in Africa. This idea is vigorously opposed, however, by the writings of Carpender (1884) and Murfin (1884).

c. Poisonous Plant Theory

Many physicians and laymen have held to the theory that trembles is caused by the ingestion of a poisonous plant. One reason for this view is the general accord of observations to the effect that "milk sick" tracts are no longer able to communicate the disease after the natural vegetation has been replaced by cultivated plants. Bennett (1822) is among the earliest writers to record this fact. He states that "those farmers who keep their cattle and horses in enclosed pastures which have been cultivated do not lose them by this disease." This opinion is also in accord with the writings of Crook (1857) and Simon (1888). Pickard (1857) cites an interesting example which substantiates the view that clearing and cultivation are efficacious in destroying the dangerous quality of milksick lands. He reports that a "family having suffered from its ravages, plowed up a pasture field, digged around the stumps, thoroughly turning all the soil, and sowed the field in grass, upon which they have kept their stock for twenty years, and at no time has milksickness made its appearance; while on other portions of the farm, uncultivated, it is as fatal as ever." The same opinion is expressed by Drake (1841), who records that "clearing and cultivation, even girdling the trees, harrowing the ground, and sowing it with grass seed destroys and renders inactive the cause, whatever it may be."

Another reason for belief in poisonous plants as the cause of trembles, is that the disease is largely limited to the season when animals are allowed to graze. That the disease may occasionally appear in winter is attested by the writings of Yandell (1852), Beck (1857), Waggoner (1859), Beach (1884), and Shapard (1892). This may be accounted for by the feeding of hay as has been recorded by Gray (1881), Beach (1883), and others. The latter makes the following interesting statement: "That cattle *may* have trembles in the winter season is a matter of occasional observation, and the old citizens generally attribute it to the feeding of cattle upon wild or swamp hay." Beck (1857) has stated that in Kentucky the disease is prevalent only in winter, whereas, in Indiana it occurs in all of the other seasons.

It seems to be the common belief among farmers in North Carolina that the usual time of prevalence is during the months of August, September, October, and November. Dawson (1842), Rawlings (1874), and Shapard (1892) refer to the greater prevalence of trembles in late summer and autumn. Dewey (1845) speaks of its disappearance after the first hard frost. While the autumnal incidence has been found to be most frequent, it may also occur during spring and early summer. An epidemic in Tennessee recorded by McCoy (1907), to which refer-

ence has previously been made, occurred during April and May. In the light of evidence to be presented later in this paper, there is no reason for believing that the disease may be limited to any one season. If it chances to be more prevalent in late summer and fall, as is commonly believed in this State, it can be accounted for by the refusal of animals to eat of the weed until this season of the year. A scarcity of more palatable plants through drought may compel them to eat more freely at this season of white snakeroot than is their custom.

A considerable number of flowering plants have at various times been held to be the cause of trembles. Among them are the following: Rhus toxicodendron (poison ivy), Eupatorium urticaefolium (white snakeroot), Lobelia inflata (Indian tobacco), Cicuta maculata (water hemlock), Bigelovia Rusbyi (rayless goldenrod), Psedera quinquefolia (Virginia creeper), Symphoricarpos orbiculatus (coral berry), Apocynum cannabinum (Indian hemp), Caltha palustris (marsh marigold), Euphorbia esula (leafy spurge), and Aethusa cynapium (fool's parsley). Through the writings of Drake (1836 and 1841), Travis (1840), Crook (1857), Chase (1861), and Elder (1874), poison ivy was at one time quite generally accredited as being the cause of the disorder. Henry (1854) and Beach (1883) pointed out that horses, cattle, and sheep frequently eat the foliage of this plant with manifestly no ill effects. The connection of poison ivy with trembles is further opposed by Landrum (1861) and H. M. K—— (1862), who assert that milksickness has never occurred in certain localities where poison ivy grows luxuriantly.

Claims that a number of other plants are the probable cause may be found in the accounts of McCall (1822), Short (1840), Fisher and Kennicott (1861), and Allen (1878), but these authors adduce little evidence in support of their conclusions.

White snakeroot has probably been more commonly accused of being responsible for trembles than any other plant. As long ago as 1840 Dr. Barbee, who will be recalled as having first given information to Dr. Drake which led to the publication of the first account of the disease, expressed the opinion that this weed was the cause of the disease. A few years later Dewey (1854) stated that the disease is due to "a succulent plant bearing a white blossom." He did not know the name of the plant and failed to have it identified, but it is very probable that he had reference to white snakeroot. Subsequently, evidence adduced by feeding experiments conducted by Vermilya (1858), Jerry (1867), Townshend (1883), and Moseley (1906) point to white snakeroot as the etiological factor in the production of milksickness.

Moseley's account, beyond doubt, contains the best experimental evidence which had been presented up to that time on the poisonous properties of this weed. His results were not entirely convincing, however, since Crawford (1908), in criticising them, states: "It cannot be said that Moseley has even proved Eupatorium urticæfolium to be a poisonous plant, much less the cause of "trembles." Beach (1883) had previously recorded the observation that cattle frequently eat this weed without any apparent ill effects.

The most extensive recent studies, except those published in a preliminary report from this Station (1917), bearing on the toxicity of white snakeroot are those of Crawford (1908), which were undertaken because of an outbreak of trembles resulting in the death of about 50 head of cattle near Minooka, Ill. Patches of white snakeroot which had been browsed were found in pastures where the animals had contracted the disease. Some of these weeds were collected and dried, while others were preserved in water to which a small quantity of chloroform had been added. Aqueous extracts were then prepared and fed or injected subcutaneously into rabbits, cats, and dogs No cases of trembles developed in these animals and Crawford became so convinced of the innocuous nature of the plant that he took without ill effect a water extract from 400 grams of fresh Eupatorium urticæfolium. These results with aqueous extracts are in accord with those secured by the present writers, and which are discussed later in this report.

Crawford furthermore reports that he fed 58 grams (about one-eighth pound) of fresh plant to a lamb weighing 25 kilograms (about 55 pounds) with the production merely of some diarrheal symptoms. In criticising this experiment, Moseley (1909) says that this quantity would probably not be fatal to a full grown rabbit. In his summary of these experiments, Crawford states "It cannot be said that it has been proved that milksickness is due to any constituent of Eupatorium urticæfolium."

The preliminary account referred to above contains the results of feeding white snakeroot to sheep during the season of 1916. Since the present season's work has been in part a confirmation of that of 1916, it is deemed best to combine all of the data bearing on any phase of the problem. These data will, therefore, appropriately appear later in this report.

Distribution and Description of White Snakeroot.

White snakeroot is a member of the composite family and belongs to a genus which is represented in the southern United States by about

forty species. The plant is also known by the common names white sanicle and rich weed, and bears the technical name Eupatorium urticæfolium Reich., which is synonymous with E. ageratoides L. f. and E. boreale Greene. The specific name indicates that the leaves resemble in appearance those of the wood nettle. This plant (Plate 1) grows in rich woods bordering streams, being confined to rather low, swampy situations, or within shaded mountain coves, particularly on northern slopes. It often grows so luxuriantly in these latter situations within North Carolina as to become the principal vegetation on the forest floor.

It is evidently very widely distributed since its range is said to extend from New Brunswick southward to Florida, Georgia, and Louisiana, and westward to Nebraska and Oklahoma.

Specimens in the herbarium of the New York Botanical Garden* show that it has been collected in Ontario, Maine, Vermont, Massachusetts, Connecticut, New York, New Jersey, Pennsylvania, District of Columbia, Virginia, West Virginia, Georgia, Louisiana, Michigan, Illinois, Indiana, Minnesota, Iowa, Nebraska, Oklahoma, and Kentucky. This would indicate that it very probably occurs in all of the other States east of the Mississippi river as could best be ascertained by examinations of the Gray Herbarium at Harvard University and of the United States National Museum.

The plant is perennial rooted, varies in height from one to five feet, and is more or less branched. The leaves are three to six inches long, opposite, long stalked, and thin. They are ovate or slightly cordate in outline, are pointed, and the leaf margin is coarsely and sharply serrate. The base of the leaf is cordate or is abruptly narrowed into a long, slender petiole or stalk. Furthermore, the leaves are strongly three-ribbed. The flowers open from July to November, and are very attractive since they are clustered in snowy white, compound corymbs. The involucre is narrowly bell-shaped or campanulate, being composed of linear, acute bracts. The achenes or seeds are smooth.

The plants are for the most part smooth, but some possess a coating of hairs. To those which are distinctly hairy, the appropriate varietal name villicaule is applied by some. Intergrading forms between the smooth and hairy forms may be found in any area where this plant occurs.

*This information was furnished through the kindness of Mr. Percy Wilson of the New York Botanical Garden, to whom thanks are hereby extended.

Comparison of White Snakeroot with Related Species

Some of the species of Eupatorium are distinguished with difficulty from white snakeroot, which accounts for the fact that farmers on being shown white snakeroot and told that it is the cause of trembles, not infrequently assert that their stock feed upon the plant without any ill effects. The casual observer cannot depend upon the color of the flowers to distinguish species, since more than thirty species of Eupatorium have white flowers. Furthermore, Eupatorium incarnatum, which may have flowers tinged with pink or purple although frequently they are white, is practically indistinguishable from white snakeroot except by the presence of minute hairs on the corolla tube. These can be seen only with the aid of a hand lens.

Twenty-nine species with opposite leaves have been described. Only seven of these, however, including white snakeroot, have manifestly stalked or petioled leaves. In this group five possess leaf blades which are similar in shape to those of white snakeroot. The leaf blades of the other one are fully twice as long as broad, which makes its separation easily possible.

Whether or not the roots are perennial is a distinguishing character, since only five species with perennial roots, in which group white snakeroot is included, have been listed. Two of these are shrubby and the other three are herbaceous. In the latter group, the character of the leaf margin, whether it be provided with sharp or blunt teeth, is used in separating E. urticæfolium from E. aromaticum, and the absence of a beard on the corollas separates these two species from the other, E. incarnatum.

The direction of attention to these points of similarity between white snakeroot and other species of Eupatorium will, it is hoped, serve to indicate that careful observation and experience are necessary in determining whether one is dealing with white snakeroot or some of the other species which are not known to be poisonous, but which are commonly present within the State.

Names of the Disease

This disease has been appropriately designated as trembles in animals, because trembling is the most obvious symptom, and as milk-sickness in man, because it may be communicated to man through milk from cows affected with trembles. It has been given a number of other names, but it is not possible because of the mystery which has for so long surrounded the cause of the malady to determine whether, in every instance, reference is made to the same disorder.

Since obstinate vomiting is such a prominent symptom of the disease in man, physicians and others have very commonly employed the name sick stomach, Beck (1822), Bennett (1822), Campbell (1881), Chamberlain (1826), Crookshank (1826), Drake (1836), Drake and Yandell (1840, 1841, 1842), Haines (1822), McCall (1830), Wright and Bennett (1827), and Yandell (1832).

The name "tires and slows," employed by Howard (1871), Logan (1849), and Byford (1855) are used in some sections. Jordan and Harris (1909) are of the opinion that "alkali poisoning" of western Texas and New Mexico is identical with trembles or milksickness in States east of the Mississippi River. Other names, which have at one time or another been employed but which have not been generally used, are swampsickness, river fever, puking fever, stiff-joints, colica trementia, morbeo lacteo, ergodeleteria, gastritis, gastro-enteritis, mukosoma, syro, lacemesis, caconemia, and paralysis intestinalis.

CLINICAL HISTORY

Symptoms

The published reports of observations by others are essentially unanimous in stating that horses and cattle are both very subject to the disease. Sheep and goats may furthermore be affected and a number of writers have asserted that hogs are susceptible. McCall (1822), Coleman (1822), Drake (1840), Winans (1840), and Davis (1881) are among those who claim that hogs are subject to the disease. Some writers have claimed that hogs are at most only rarely affected—Woodfin (1878) and Johnson (1866). It has been stated, too, that deer may suffer from the disease, and that other wild animals, such as wolves, foxes, buzzards, vultures, and crows may contract trembles by feeding upon carcasses of animals which have died of this disease.

a. In Cattle.—The symptoms of trembles among domestic animals have been described with no great degree of fullness except in cattle. The following account is substantially a concensus of all who have observed the malady. The first sign of the disease is indicated by a listlessness and disinclination to move. In his memoir, Drake (1841) has well characterized the initiation of trembles by stating that "the animal begins to mope and droop, to walk slower than its fellows, to falter in its gait." Practically all accounts record the exhibition at this stage of muscular weakness and of trembling, especially when the animal is driven. Such animals, too, are generally constipated. Some few writers record that cattle in this stage are greatly excited and are disposed to fight; this is not mentioned, however, by the great majority

of observers. When the disease has progressed sufficiently so that the characteristic trembling ensues, there is a marked stiffness of the joints. The animal may sink to the ground manifesting great weakness and exhaustion, and may remain lying for hours or days on the spot where it has fallen. Animals in this stage may recover, but more often die.

One peculiar feature of the disease, *i. e.,* that violent exercise has much to do with the development of acute symptoms, has been generally reported and is in accord with statements by a considerable number of farmers within the State. Prospective buyers of cattle from "milksick" areas make use of this fact and drive the cattle until they are heated before deciding whether it is safe to purchase. Dixson (1833) early noted this and says "It is one of the peculiarities of the disease that the poison lies long dormant in the system, and only becomes active when excited by some indiscretion or violent bodily exertion." Woodfin (1873) states that "beeves have been fattened in these infected localities, started to be driven to market, take the trembles and fail the first or second day, while other cattle feeding on the same grounds, left at home, remain healthy."

This is entirely in accord with observations made by Mr. W. R. Radford and Mr. James Phillips in Mitchell County, at Spruce Pine, N. C., during the present year. Mr. Phillips purchased a herd of 20 steers and heifers which had pastured in Wiggins' Cove, on the farm of Mr. S. T. Henry, where white snakeroot grows profusely. The animals were driven to the shipping station, several miles distant, and upon arrival at the station five began to tremble. They remained lying down most of the time for several succeeding days, and when made to rise would stagger along for a short distance and then fall suddenly. They had all apparently recovered, however, after about a week.

The belief, which prevails in some sections, in the occurrence of the disease in the autumn only, may be accounted for in the light of this peculiar fact, if it is kept in mind that in these places it is the practice to drive cattle to market at this season of the year.

Another peculiarity which has been recorded by a number of observers is that the breath of affected animals has a foul odor. This has been described as "garlicky," "like chloroform liniment," and "mildly like acetone." Elder (1874) speaks of it as a "singular fetid odor, pungent, and corrosive."

The fact that not all cattle in the herd become affected has always been a disturbing factor in accounting for the cause of trembles. As long ago as 1822, Coleman notes that "Cattle and horses do not always become afflicted with the disease if allowed to range in woods where the disease is common." Woodfin's (1878) comments bearing on this point,

if judged in the light of experiments with sheep to be presented later, are equally true and interesting. He says: "Many animals may feed on the same lands and evidently partake about equally of the poison and some of them suffer violently and die; others suffer lightly and recover, and others still, perhaps the larger number, remain quite healthy."

b. In Sheep.—Very little that is distinctive can be gathered from the published accounts of the symptoms of the disease in other domestic animals. Writers have largely resorted to the use of the expression "similar to those of the disease in cattle" in describing the symptoms.

The only clinical account of the disease in sheep which has come to our attention is that given by Jordan and Harris (1909) from observations made by D. D. Todd upon two ten weeks' old lambs. Both of these animals were lying down when found, and one made no attempt to rise, while the other kept its feet going in a walking motion with each unsuccessful effort to get up. Respiration was regular in both animals but forced and jerky in the case of one lamb. No sign of pain was evident, but occasionally one animal ground its teeth.

In the present studies in sheep considerable individual variation has been found to exist, both in the period elapsing until the initial symptoms of trembles are apparent and in the period following until death ensues. During the season of 1916 some were sick as early as three days after being placed on the experiment, and no ill effects were apparent for three weeks in other cases. During the present season (1917) one animal became sick on the second day and died within forty-eight hours after feeding was begun. Others remained apparently normal for about twelve weeks before contracting the disease. Sheep usually live three or four days after the disorder is first noticed, but some have been observed to die within twelve hours. Only one sheep characteristically affected entirely recovered and the feeding of white snakeroot to this animal was discontinued as soon as trembling was noted.

One of the first signs of the onset of the disease is a loss of appetite and gritting of the teeth. Such animals are sluggish and manifest a marked disinclination to move. They may remain standing in a droopy posture (Fig. A) or may be quiet in a normal resting position. Respirations are accelerated, often jerky and somewhat labored. A marked stiffness of the legs and ataxia characterize the movements in walking. This is manifest early and becomes more aggravated as the disease progresses. If after a day or two, the animal is urged to rise and is driven a few yards, muscular spasm, especially in the limbs, is evident. The sheep then refuses to move, stands with hind limbs placed well under the body (Figs. A and B) and all feet spread apart laterally. In this

posture, the back is bowed, the neck outstretched and the head lowered. Within a few seconds, the quivering spreads from the limbs over the entire body, increases in intensity, and becomes a violent, involitional tremor (Fig. B). This is accompanied by slight, intermittent, tetanic contractions of the musculature of the limbs. At this stage of trembling ataxia is very pronounced, and the animal is unable to stand (Fig. C). It drops quickly into the normal resting posture (Fig D) or assumes a characteristic position, in which the head and neck are outstretched and the jaw is resting upon the ground (Fig. E), whereupon the trembling apparently immediately ceases. If the sheep is made to rise after it has lain down for a few moments, a second and more violent spasm of trembling ensues with a repetition of the symptoms as described. Trembling may recur repeatedly every time the animal is made to rise. The quiescent period is shortened, however, after each spasm of trembling and may begin as soon as the animal is placed on its feet. Even after the disease has progressed to the point where trembling is violent, many animals still possess considerable appetite.

After the second or third day, the animal becomes comatose and may lie prostrate on its side (Fig. F) until death occurs. There is generally a very considerable decrease in weight, most of which occurs during the two or three days preceding death. The feces generally remain normal, with, in some cases, a small amount of mucus. Urination is more frequent than in healthy animals and only a small quantity is voided each time. Vomiting occurred in the case of two animals under observation, and a frothy discharge from the nostrils is not uncommon after coma sets in.

c. In Hogs.—The symptoms of trembles as observed in hogs are in general like those in sheep. There is first a listlessness, not accompanied, however, by any marked loss of appetite. The animal remains lying unless urged to rise, or unless food is offered, whereupon it stands with hind feet placed well under the body. In this position, the head droops, the eyes are partially closed, and the back is bowed. (Fig. I.) There is no lack of coordination of movement in walking for the first few days, although the hind legs are markedly stiff. Later, this stiffness appears in the fore limbs. After the pig has stood for a few minutes while eating at the trough or is driven around in the pen a slight quivering in the legs begins. Within a few moments, the trembling has become progressively more severe, has spread over the entire body and becomes a violent shaking or tremor, so acute that the animal squeals, presumably with pain, in its efforts to remain on its feet. At this stage of trembling the animal either falls to its knees or sits upon its haunches (Fig. J). From this position, after a moment, it falls into

the resting position (shown in Fig. K), in which the feet are folded under the body and the jaw resting upon the ground, or it falls prostrate on its side with legs outstretched (Fig. L). Trembling continues for some little time after the animal has lain down.

Three or four days after trembling is first noted, it is not uncommon for the animal to topple from a standing posture to one flat upon its side. Coma appears in the 24 or 48 hours preceding dissolution.

d. In Guinea Pigs.—The disease is first apparent in guinea pigs by their refusal to eat. They are less active than unaffected animals and crouch in a corner of the cage. The hair upon the head and neck of sick animals does not lie down smoothly and their eyes remain only partially open. When such an animal is disturbed, it walks with the back arched. As the disease progresses, they become more listless, refuse all food, and become emaciated in consequence. Commonly diarrheal symptoms are present. Muscular tremors occur, but are not easily apparent since the animals cannot be made to stand nor to walk. Finally stupor sets in, at which stage they are very limp, with insufficient control of their limbs to enable them to rise when placed on their side. The half-closed eyes and general debility as indicated by the droop of the ear and posture are shown in a comatose animal in Fig. H.

e. In Man.—Several excellent descriptions of milksickness in man have appeared, in all of which the symptomatology appears to accord fairly uniformly. In the accounts of Coleman (1822), Graff (1841), Byford (1855), and Way (1893), attention is directed to the most typical symptom, "sick stomach."

The onset of the disease is gradual, and after a day or two of weakness and debility, accompanied by loss of appetite, the patient is seized with epigastric distress. Excessive vomiting follows, the bowels are obstinately constipated, and there is always great thirst, although the water taken is vomited immediately. Abdominal pain is generally present, although some writers record an absence of distress in this region, and muscular tremors are generally present. The breath acquires a peculiar foul odor, a characteristic which some regard as of great diagnostic value, since they maintain that it can be detected immediately upon entering the patient's room. The tongue is swollen. Respiration is normal and temperature is usually subnormal, ranging from 97 to 98 degrees F., although McCall (1822), Simon (1875) and a few others state that fever exists. If the disease is severe, symptoms of typhoid may appear. The patient may become delirious, but in fatal cases a period of coma precedes dissolution. In such cases, death may come as early as two days after the onset of symptoms or may be deferred for two or three weeks. Lasting debility appears to be a common sequel

of the disease. Those who have recovered are usually incapacitated for hard work especially during warm weather. The writers themselves have never seen a person suffering from milksickness, but conversations and correspondence with doctors who have treated cases, and with persons who have recovered from an attack, indicates that the preceding account of symptoms describes the disease.

Mortality in Trembles or Milksickness

No data are available from which even an approximation of the fatalities among domestic animals can be made. One writer has estimated that 5,000 animals have died from the disease in a certain area in northern Ohio. The outbreak near Minooka, Ill., which occasioned the investigations of Crawford (1908), previously referred to, resulted in the death of about fifty cattle. Mr. H. E. Crawford, Shooting Creek, N. C., reports the loss of hundreds of dollars worth of horses, cattle, sheep, and hogs, and that in almost every case affected animals succumbed.† In a flock of sheep which came under the observation of Mr. George Evans, Sheep Field Specialist at this Station, seven animals in a flock of eight died. In our feeding experiments with sheep, only one individual characteristically affected recovered among a total of thirty-one animals. In the succeeding year this animal was again used in feeding experiments and contracted the disease and died. All accounts which have come to hand, both published and verbal, indicate that relatively few animals recover from a prolonged attack of trembles.

The data on the mortality in man from milksickness are by no means complete and considerable differences of opinion are found to exist in published reports. Coleman (1822) reports the loss of "about one case in twenty or thirty," and Collins (1902) "about 40 per cent of my cases." Dr. J. E. Wilson, Canton, N. C., informs us that he has treated many cases without the loss of one.

Jordan and Harris (1909) have prepared a tabulation of all published reports in which the number of cases and deaths is specifically stated. This tabulation will emphasize the variation which has been mentioned and will give at least an approximation of the average mortality. It will, therefore, be quoted *in toto,* and to it will be added the record of fifty-six cases and eleven deaths which either came under the observation of Jordan and Harris or were reported to them during their investigation of this disease, and of two deaths at Losantville, Indiana, in 1916.*

†From a letter by Mr. E. S. Millsaps, County Agent, Clay County.
*From a letter by Dr. N. F. Canady, Hagerstown, Indiana.

Cases	*Deaths*	*Authority*
4	2	Lewis (1829)
10	5	Carney (1847)
1	0	McNutt (1857)
49	26	Sale (1871)
50	7	Smith (1867)
30	0	Smith (1874)
3	2	Houser (1880)
22	4	Spalding (1881)
3	1	Gray (1881)
4	2	Simon (1888)
11	6	Pusey (1880)
6	5	Graff (1841)
9	5	Tuller (1889)
2	0	Scott (1889)
6	1	Hurd (1875)
13	2	Sykes (1891)
6	1	Lyday (1896)
9	1	Mich. S. B. H. (1897)
5	2	Collins (1902)
13	6	Palmer (1904)
6	6	McCoy (1907)
56	11	Jordan and Harris (1909)
2	2	Canaday (1916)
320	77	

The mortality in man as judged by these data is seen to be approximately 24 per cent.

EXPERIMENTAL PROCEDURE

Since white snakeroot does not grow in the vicinity of Raleigh, N. C., where these feeding experiments were conducted, it was arranged to secure daily shipments of the green weed from Shooting Creek, N. C., where this plant grows luxuriantly. Since this town is over 400 miles distant from Raleigh, the weed used had been collected about 48 hours prior to its arrival at Raleigh. The weed was fed twice daily along with a maintenance ration of some dry concentrate. In the feeding experiments of the present season (1917) this feed was further supplemented by timothy hay. The sheep were kept singly in small pens in a sheep barn. A litter of shavings covered the concrete floors. The animals used were selected from a flock of grade ewes and their lambs, all of which were in a healthy condition, and, with the exception of those used in the experiments, remained so. No case of trembles or milksickness had ever appeared in this or any other of the Station flocks prior to the initiation of these experiments and none developed

during the course of these experiments except in animals under experimentation. The flock number of each individual was retained and is used subsequently in reporting the experiments with the several animals.

At first the grain and weed were fed separately; but since the animals either avoided eating any of the weed or ate only sparingly of it, the weed was passed through an ensilage cutter and then mixed with grain before being fed. A daily account was kept of all of the feed which was refused by each animal, and these data were employed in approximating the total amount consumed during the course of the experiment. Since the weed and grain were mixed, and since some loss of weight was due to desiccation, the quantity of snakeroot eaten by each animal could only be approximated.

In the experiments with suckling lambs, the ewes and their lambs were kept separated except while the lambs took their milk. The ewes at these times were put into the pens with the lambs, so that the lambs never had access to white snakeroot, as would have been the case had the lambs been permitted in the ewes' pens.

Before feeding the weed to pigs, which were confined in pens in the sheep barn, it was passed through an ensilage cutter and mixed with cracked corn and shorts.

The dogs, which were fed upon the carcasses of sheep dead of trembles, were confined in pens and given, in addition, dog biscuits and refuse from the kitchen.

The guinea pigs which were used in these experiments had never been used in experimental work and were consequently entirely normal. During the experimentation they were kept in cages especially constructed for housing small animals, and were given a diet consisting of a mixture of cracked corn, wheat, oats, and rye, which was supplemented by green grass and clover. All animals used in any one of the experiments to be subsequently reported were kept together in the same cage. Each group of animals could thus conveniently be fed twice or three times daily with white snakeroot or some of the products prepared from this plant.

The material extracted by boiling the plant in water, in 2 to 3 per cent hydrochloric acid, or alcohol, for twenty-four to forty-eight hours, was evaporated to dryness on a water bath, ground into powder, and placed in No. 2 Lilly New Process Gelatine Capsules. The desiccation of these products necessitated heating for a long time because of the resinous nature of the extracted material.

The animals were held while feeding them these capsules, and were given from six to twelve capsules daily. By the exercise of considerable patience, the guinea pigs could be made to masticate and swallow the

capsule and its contents. This method of administering the products of white snakeroot was abandoned for a more convenient one in the other experiments. All materials not already in liquid form were dissolved in water and were allowed to drop from a pipette into the guinea pigs' mouths.

In expressing the sap or juice from white snakeroot, use was made of a small meat chopper. The green weeds were passed through this meat chopper which had been fitted with a plate having small openings. The rotation of the cylinder which fed the machine pressed the macerated weeds through these small openings and at the same time pressed out the plant sap. The sap escaped through the crevice between the rotating cylinder and the frame of the chopper, that is, in the direction opposite that in which the "pomace" or residue escaped.

Post-mortem examinations were made of twenty-two of the thirty-one sheep which died of the disease. Thirty of these animals were observed to tremble in the characteristic manner. With the exception of ewe No. 169 and lamb No. 237, both of which had stomach worms (Hemonchus contortus), there was no evidence that death resulted from causes other than the feeding of E. urticæfolium. Both of these animals manifested characteristic symptoms of trembles, however. Post-mortem examinations were furthermore made of all other animals which died during the course of the experimentation and certain of the internal organs were also preserved for microscopic study. A detailed report covering studies on some of these tissues has been prepared and is representative of all cases examined.

RESULTS OF EXPERIMENTS

a. With Sheep

Experiment 1.—Three ewes, Nos. 11, 26, and 10, were used in Experiment 1, a preliminary experiment which was designed to determine whether harmful effects follow the feeding of E. urticæfolium. This experiment was begun on June 17 and closed on August 2. However, from June 22 to July 6 and from July 18 to July 28, it was impossible to secure the weed. During these periods the animals were grazed on Bermuda grass pasture. Except during the two periods mentioned, a liberal supply of white snakeroot was fed just as it arrived from the point of shipment. In addition, a maintenance ration of grain was fed in a separate trough. Neither the weeds nor the grain were weighed in this experiment. Initial and final weights of each animal were recorded.

In the period between June 17 and July 16, ewe 11 was fed on white snakeroot and grain for an aggregate of fifteen days. A typical case

of trembles had developed by July 16, and death occurred two days later. Food was refused during these two days, and there was a decrease in weight from 102 to 77 pounds during the 29 days of intermittent feeding.

Ewe 26 was given a ration of snakeroot and grain for 22 days, between June 17 and August 2. No symptoms of trembles developed during this period. The initial weight of this animal was 91 pounds and the weight at the time the experiment was discontinued was 74 pounds.

The control ewe (No. 10) was maintained on pasture alone from June 17 to July 28. On July 28 she was put in a pen and was given a ration of white snakeroot and grain until her death, which occurred on August 2. This ewe trembled only slightly, was very weak and emaciated, and lost 20 pounds during the experiment. Although the symptoms were not as marked in this case as in ewe 11, yet all conditions indicated that death was due to trembles.

Experiment 2.—Three ewes, Nos. 14, 23, and 26, were employed in Experiment 2. This experiment was planned to confirm the results secured in Experiment 1. Since the animals used in Experiment 1 had refused to eat any considerable quantity of snakeroot when it was fed separately, it was decided to pass the weed through an ensilage cutter and mix it with an equal quantity of weight of grain. One pound of this mixed feed was given each animal twice daily.

On the sixth day after ewe 14 was placed on the experiment she had developed trembles and died on the following day. Her initial weight was 80 pounds and her weight at death was 73 pounds.

The first symptom of trembles in the case of ewe 23 was noted 19 days after the experiment was begun. A well-defined case of trembles developed in this animal, and she died six days after the first symptoms were noticed. Her weight when feeding was begun was 70 pounds, and there was a loss in weight of 8 pounds during the 25 days.

Since ewe 26 had shown no ill effects from the feeding of white snakeroot in Experiment 1, she was used in this experiment. It will be recalled that the weed was fed separately and was not ground in the first experiment. Ewe 26 had eaten only sparingly of the weed in this experiment. However, after 16 days feeding with the mixed ration, a very typical case of trembles developed. The feeding of the weed was therefore discontinued and she was put on pasture.

Experiment 3.—In this experiment, ewes 12, 7, 29, 27, and 19 were fed the mixed ration to determine the amount of weed and the length of time required to develop trembles. Table 1 shows clearly the variation that exists with reference to these two points.

TABLE I—RESULTS OF FEEDING WHITE SNAKEROOT TO SHEEP IN 1916. EXPERIMENT 3.

Ewe No.	*Initial weight.*	*Experiment begun.*	*Feeding discontinued.*	*Days before death occurred.*	*Weight at death.*	*Feed consumed*	
						Grain	*Weed*
	Pounds.				*Pounds*	*Pounds.*	*Pounds.*
12	74	August 5	August 18	13*	....	5.5	11.5
7	86	August 5	September 1	27	61	13	9
29	81	August 5	August 21	16	55	8	10
27	70	August 5	August 10	5	56	2.25	4.5
19	113	August 5	August 23	18	89	8	11.25

*Feeding discontinued after thirteen days.

Ewe 12 was taken off the experiment on August 18, at which time she was affected with trembles. She had lost only 1 pound during these 13 days. It will be noted that the amount of weed required to cause trembles in these five animals varied from 4½ to 11½ pounds and the range in time from 5 to 27 days.

Experiment 4.—In order to determine whether or not trembles is infectious, ewes 26 and 12 were put in a small Bermuda grass lot on August 18. Two healthy ewes from the flock were put in the same lot and all were fed grain in the same trough. It will be recalled that both ewe 26 and ewe 12 had typical cases of trembles when their feeding in experiments 2 and 3, respectively, were discontinued. Ewe 26 died on August 19 and ewe 12 still trembled a week afterward. However, she finally recovered fully. Neither of the other two ewes had developed any symptom of trembles when the experiment was discontinued on September 4, and both subsequently remained normal. It is realized that this indirect evidence of the relationship of a specific infection is in itself not convincing so that in studies to be subsequently reported an effort was made to isolate an organism from the internal organs of affected animals.

Experiment 5.—This experiment was designed to determine the length of time that white snakeroot must be fed to sheep when, after a certain number of days the usual grain ration and pasturage are given. Two animals were therefore fed for three days on a mixture of equal parts of ground weed and grain and were then put on pasture. Two others were fed for six days before being placed on pasture and two others for nine days, after which they were put on pasture. Table II contains the essential facts in this experiment.

TABLE II—RESULTS OF FEEDING WHITE SNAKEROOT TO SHEEP IN 1916. EXPERIMENT 5.

Ewe No.	*Initial weight. Pounds.*	*Final weight. Pounds.*	*Days on experiment.*	*Feed consumed.*	
				Grain.	*Weed.*
169	83	78	3	1.5	1.5
171	85	80	3	1.5	1.5
162	96	82	6	5.5	5.5
168	89	79	6	4.25	4.25
161	102	62	9	6.75	6.75
170	105	92	9	5.5	5.5

Ill effects followed only in the cases of ewes 169 and 161, the former dying 8 days and the latter 11 days after being taken off the experiment. Since ewe 169 evidenced no well marked symptoms of trembles, a post-mortem examination was made which showed that stomach worms may have been a contributory cause of her death. Ewe 161, however, developed a typical case of trembles and is the animal represented in figures A, B, C, and D.

Experiment 6.—The preceding experiments, which were conducted in 1916, had demonstrated the poisonous nature of white snakeroot. Attention was therefore first directed in the succeeding year to determine by experiment, first, if the disease can affect animals in lactation, and second, if these animals can transmit the disease through the milk to their offspring. For this purpose, six ewes with suckling lambs were employed in an experiment which was begun May 13, 1917. The facts brought out in the second part of this experiment are properly referred to Table VI and will, therefore, appear in their appropriate place later in this report. The data bearing on the first point, however, are summarized in Table III, which is presented as follows:

TABLE III—RESULTS OF FEEDING WHITE SNAKEROOT IN 1917 TO EWES WITH SUCKLING LAMBS. EXPERIMENT 6.

Ewe No.	*Initial weight. Lbs.*	*Experiment begun.*	*Date of death.*	*Days before death occurred.*	*Weight at death. Lbs.*	*Gain or loss. Lbs.*	*Feed given.*			
							Grain. Lbs.	*Weed. Lbs.*	*Kale. Lbs.*	*Hay Lbs.*
171	76	May 13	Aug. 30	109	88	12	162	54	134	106
162	81	May 13	Sept. 2*	111	88	7	163	55	134	108
175	83	May 13	Sept. 2	111	98	15	165	55	134	108
167	104	May 13	Aug. 20	99	105	1	132	44	132	96
12	94	May 13	July 24	72	97	3	103	34	134	69
168	80	May 13	July 15	63	74	6	80	27	124	60

*Discontinued feeding white snakeroot at this date.

It will be noted that four of the six ewes developed trembles and died while on this experiment, and that two were apparently normal when the feeding with white snakeroot was discontinued. Only meagre quantities of milk were being given by these animals after July 1. Ewes 168 and 12 died on July 15 and July 24, respectively, at which times their

lambs were still alive. Ewe 167, which died August 20, had not suckled her lamb since July 25, and Ewe 171, which died August 30, had not suckled her lamb since June 15.

It should further be noted in this experiment, as well as in experiments 7 and 8 which follow, that the figures representing the quantity of weed given do not represent the quantity actually eaten, since the ewes consistently attempted to avoid eating any of the white snakeroot. Very much smaller amounts would have produced death, had they eaten as much as a pound daily for several days. It is furthermore believed that the liberal quantities of grain, kale, and hay which were given to stimulate the flow of milk, perhaps by absorbing the toxic principle, rendered it less active.

Experiment 7.—It was planned in this experiment to duplicate Experiment 6 in its entirety with ewes in lactation and suckling lambs. The period of lactation was so far advanced, July 7, when the experiment was begun that none of the lambs contracted milksickness, in consequence of which the detailed report of this part of the experiment is withheld. The results of feeding white snakeroot to the mothers, however, will be assembled in Table IV.

TABLE IV—DATA BEARING UPON THE FEEDING OF WHITE SNAKEROOT TO EWES IN LACTATION, IN 1917. EXPERIMENT 7.

Ewe No.	*Initial weight. Lbs.*	*Experiment begun.*	*Date of death.*	*Days before death occurred.*	*Weight at death. Lbs.*	*Gain or loss. Lbs.*	*Feed given.*			
							Grain. Lbs.	*Weed. Lbs.*	*Kale. Lbs.*	*Hay Lbs.*
31	104	July 7	Aug. 28	52	102	—2	77	26	26	52
22	81	July 7	Sept. 2*	56	83	—2	78	27	26	56
17	93	July 7	Aug. 6	30	95	2	39	14	26	30
15	93	July 7	Sept. 2	56	95	2	79	27	26	56
9	94	July 7	Aug. 22*	46	104	10	65	22	26	46
16	135	July 7	Aug. 22*	39	140	5	63	20	26	47

*Feeding was discontinued on the date indicated.

Three of the six ewes employed in this experiment died. Ewe 31 was discontinued on this experiment, however, August 20, and is subsequently reported in Experiment 11, on which she died August 28. Ewe 16 was discontinued on August 15 and is reported in Experiment 9, which resulted in her death August 22. Ewe 17 alone, which died August 6, ate most of the weed given and developed a typical case of trembles, whereas the weed given to the others was for the most part refused. Ewes Nos. 22, 15, and 9 were placed on pasture at the time of discontinuance of the experiment.

Experiment 8.—This experiment was begun on the same date as Experiment 7, in order to determine whether animals not in lactation be-

come affected with trembles earlier than those in lactation. Here again, six animals whose lambs had been weaned were selected. The data bearing on this experiment are presented in the following tabulation:

TABLE V—RESULTS OF FEEDING WHITE SNAKEROOT TO EWES WITH WEANED LAMBS. EXPERIMENT 8.

					Feed given.			
Ewe No.	*Initial weight. Lbs.*	*Experiment begun.*	*Date of death.*	*Days before death occurred.*	*Grain. Lbs.*	*Weed. Lbs.*	*Kale. Lbs.*	*Hay. Lbs.*
25	104	July 7	Sept. 2	56	79	27	24	55
158	108	July 7	Sept. 2*	56	81	27	24	55
149	98	July 7	Sept. 2*	56	81	21	24	55
163	102	July 7	Sept. 2*	56	73	27	24	55
173	105	July 7	Aug. 24	48	68	23	24	47
172	85	July 7	Sept. 7*	56	81	28	24	55

*The feeding of white snakeroot was discontinued at this date.

It may be noted above that ewe 173 died after having been on the experiment 48 days, and ewe 25 after 56 days. Both had typical cases of trembles, whereas the others remained apparently healthy when the feeding with white snakeroot was discontinued, September 2. Since the period of lactation of the ewes in Experiment 7 was so far advanced and since so few deaths occurred in both experiments 7 and 8, no conclusion can be drawn as to the influence of lactation upon the period of resistance.

Experiment 9.—Four lambs and one sheep were used in this experiment to test the toxicity of expressed sap. Lamb 237 was given 500 c.c. in the afternoon of July 30. On the morning of the following day it was given 500 c.c. and an equal quantity in the afternoon. This animal had been given 1500 c.c. and was found dead on the morning of August 1.

Lamb 241 was given 250 c.c. on July 30 and two quantities of 250 c.c. on July 31. She refused to eat oats on the morning of August 1, and was given no more plant juice until the evening of August 3, when she again appeared normal. At this time, she was given 250 c.c. On each of the two succeeding days she was given 500 c.c., making a total of 2,000 c.c. She refused to eat on the morning of August 6 and trembled when made to rise. Feeding with juice was therefore discontinued, and she died on August 9.

Lamb 231 was given daily three feedings of juice of 250 c.c. each beginning on the evening of August 6. Only 250 c.c. were given on August 10 and 500 c.c. on August 11. This lamb had received 4500 c.c. by the evening of August 13, when symptoms of trembles were manifest. Trembling was violent on the following morning and the animal died during the afternoon.

Two feedings of juice of 250 c.c. each were given daily to lamb 240. This test was begun on the evening of August 6 and was discontinued on the evening of August 13. On August 10 only half the quantity was given so that the lamb had consumed 3,000 c.c. by August 13. The animal trembled on the morning of August 14 and the tremors had become so intense by evening that it could not stand. Death occurred during the night of August 14.

Between the evening of August 16 and the evening of August 22, ewe 16 was given a total of 7,250 c.c. of expressed juice. She was sick on the evening of August 22, as noted by the characteristic standing posture. On the following morning, she stood with head lowered and with mouth held open and panted for breath. She seemed to be suffering severe abdominal pain as evidenced by efforts to vomit and constant movement of the hind limbs. Death resulted at about 4 P. M. on August 22.

Experiment 10.—This experiment with lambs 233 and 222 corresponds to Experiment 21 with guinea pigs. Expressed juice was kept on a water bath maintained at a temperature of about 60 degrees C. The decrease in volume due to evaporation was restored by the addition of water. Lamb 333 was given 500 c.c. daily in two feedings beginning on the evening of August 6. None was given on August 11. She was first noticed to tremble on August 17 and feeding was discontinued. This animal was given a total of 5,000 c.c. Death took place August 18. The feeding of lamb 222 was begun at the same time, she being given 750 c.c. daily except on August 11, when none was given. Trembling was first noted on the morning of August 25 and she died during the night of August 29. No juice was given after August 24, and she received a total of 9,250 c.c.

Experiment 11.—The residue from which the volatile oil had been distilled was given to ewe 31 beginning August 20. By the evening of August 22, 3,800 c.c. had been given. None was given on the two succeeding days, and at noon on the 25th trembling was noted. Death occurred during the night of August 27.

b. With Hogs

Experiment 12.—The purpose of this experiment was to determine whether hogs are subject to ill effects following the feeding of white snakeroot. Accordingly, two animals were given this weed along with a ration of grain and shorts beginning June 21. They consistently refused to eat any considerable quantity of the weed even though it was mixed with moistened grain and shorts. One animal, however,

contracted trembles on September 24 and died six days later. This animal is shown in figures I, J, K, and L in the accompanying illustrations. The other animal remained unaffected.

c. With Guinea Pigs

Experiment 13.—On June 26, three guinea pigs were placed on an experiment which was designed to show whether guinea pigs are subject to poisoning by the ingestion of green leaves of white snakeroot. No. 1 aborted on July 1, refused all feed on that day and on the following day, and was found dead on the morning of July 3. The autopsy showed that death very probably resulted from abortion. No. 2 also aborted on July 1, but her appetite remained quite normal until her death which occurred on July 4. She was very inactive, however, during this period, but exhibited no other indication of being affected. Abortion resulted on June 29 in the case of No. 3. She ate sparingly during suceeding days and remained humped up with eyes partially closed. Upon being disturbed, she appeared quite active. On July 6 a period of coma began and death resulted on July 9. Two more animals, No. 4 and No. 5, were placed in this cage on July 3. On July 9 No. 4 was very sick and breathed with difficulty. She became comatose and was found dead on the morning of July 11. No. 5 appeared normal until July 10 and was very inactive thereafter until her death on July 23.

Experiment 14.—Beginning June 26, two male guinea pigs were fed on green stems of white snakeroot to determine if stems are as poisonous as leaves. No. 1 was noted to be droopy on the morning of July 3 and was dead forty-eight hours later. No. 2 was first noted to be affected on July 7. He then appeared listless, refused entirely the green stems and ate only sparingly of the grain. By July 9 respirations were labored, and he sat crouched in the corner of his cage. His eyes were half-closed, his ears drooped, and his head drooped. By July 11 his body was limp and he had so lost control of his legs that when lain on his side, he could not regain his feet. At this stage, trembling was apparent. The symptoms exhibited in No. 2, which animal is shown in Fig. H, are typical of trembles in guinea pigs as developed throughout these experiments. This animal was asphyxiated on July 11 and an autopsy immediately made.

Experiment 15.—At the same time that the above experiments were begun to determine whether the leaves and stems are toxic to guinea pigs, the feeding of two animals on an aqueous extract was also begun. On June 28, some diarrheal symptoms were present, which persisted

until July 5. They ate ravenously, however, and by July 8 had eaten the water soluble material from 1800 grams of dry white snakeroot with no ill effect except the disgestive disturbance mentioned. For the next fourteen days they were given an aqueous extract prepared from the fresh weed. At the end of this time, they were in good condition and the feeding was discontinued. It does not appear from this that the active principle is water soluble, or if it is, the heat of desiccation destroys its toxicity. It will be recalled in this connection, that the feeding of aqueous extracts previously reported by Crawford (1908) were not followed by trembles.

Experiment 16.—The feeding of three guinea pigs with material extracted with dilute hydrochloric acid was begun on June 28. This extract was made neutral with sodium hydroxid with the consequent precipitation of salt. No. 1 was sick on July 2, was very inactive on July 3, but ate of the grain and clover. He refused to eat on the morning of the following day, and died at noon. The other two were still unaffected on July 8 when feeding was discontinued.

Experiment 17.—The feeding of alcohol soluble products was begun on the evening of July 3. By the evening of July 5, two guinea pigs had eaten the extract from 1,800 grams of dry weed. No ill effects whatsoever followed during the succeeding two weeks in which they were kept under observation.

Experiment 18.—In this experiment six guinea pigs were given by means of a pipette the expressed sap or juice of white snakeroot. On the evening of July 20, two large animals, each weighing nearly 800 grams, were given 10 to 12 c.c. apiece. On the following morning both were noted to be droopy and refused to eat. No. 1 was so weak that he could scarcely walk and seemed unable to control the movements in the hind limbs. Each was given about 12 c.c. on the morning of the 21st and an equal quantity at noon. At 5 P. M. No. 1 died, having been given a total of about 35 c.c. No. 2 was given two feedings on the 22d and had received a total of about 50 c.c. during the three days of feeding. He became more inactive and listless daily, passed into a state of coma and died July 26.

On the morning of the 24th two more guinea pigs were placed in this cage and each was given in three feedings about 25 c.c. Both were sick on the following morning, but were given during the day three quantities of expressed juice totaling about 25 c.c. for each animal. On the following morning No. 3 died. No 4 was fed three times daily on the 26th, 27th, and 28th. Feeding was discontinued on this last date and he died three days later.

On the afternoon of the 26th another animal, No. 6, was placed in this cage, was given 16 to 20 c.c. daily in two feeds and died on August 14. No. 6 remained quite normal throughout this entire period except for two or three days prior to death.

Experiment 19.—In this experiment the expressed sap was reduced to dryness over a water bath, the water in which was kept boiling. On July 11 one animal was placed on this experiment, and given daily the equivalent of 25 to 30 c.c. of freshly expressed juice. No ill effects had appeared on July 20, when feeding was discontinued.

This animal along with two others was again placed on the experiment on July 26. Each was given daily quantities equivalent to 25 or 30 c.c. of fresh sap. Since no ill effects had appeared by August 14, the feeding was discontinued. When it is remembered that the sap was toxic before it was desiccated and that each animal had received the equivalent of many times more of fresh juice than was necessary to produce death, it is evident that desiccation at high temperature either destroys the toxicity or that the active principle had been volatilized.

Experiment 20.—This experiment was designed to show whether a toxic volatile principle is present in the sap of white snakeroot. Accordingly, 5,800 c.c. of expressed sap were distilled in a flask over an open flame. A turbid distillate was collected which contained a very pungent volatile oil. This distillate was fed to three guinea pigs beginning August 14 and concluding August 29. No ill effects whatsoever were apparent. The materials which remained after distillation were fed to ewe 31 and have been reported as Experiment 11 along with the feeding experiments with these animals.

Experiment 21.—The expressed sap fed to the three animals on this experiment had been kept for forty-eight hours on a water bath maintained at 55 to 60 degrees C. This temperature was found to be sufficient to drive off the volatile oil and was believed to be hot enough to prevent fermentation yet not a sufficient degree of heat to change the chemical constitution of the plant juice. The feeding of two animals, thrice daily, was commenced at noon on July 30 and of another on August 3. One of the first two was observed to be sick on August 2. This animal died on the afternoon of August 4. The other two continued to eat their food, however, and were merely less active than normal individuals throughout the remainder of the time that they were maintained on this product or until August 23.

TRANSMISSION OF THE DISEASE.

a. By Milk and Milk Products

In sections where milksickness prevails, it is firmly believed the disease is acquired through the use of milk from cattle affected with trembles. There seems, moreover, to have been little doubt of this fact in the minds of early settlers in the Middle West and more or less evidence has been presented in published accounts by McCall (1822), Lewis (1829), Barbee (1840), Logan (1849), Yandell (1852), Philips (1857), Cosby (1866), Nichols (1876), Woodfin (1878), Sykes (1891), Beck (1905), and McCoy (1907), in the several medical journals.

An instance of an apparent exception came under the observation of Jordan and Harris (1909) during the summer of 1908. Four cases of milksickness in a family of ten developed near Altamonte, Ill., on a farm which had "long been known to give rise to milksickness." In discussing the occurrence, they state that "The cows were to all appearance entirely healthy, and showed no signs of disease before or after the outbreak; a six-to-eight weeks old calf whose mother was one of the animals providing the milk used in the family also seemed in the best of condition. A cat that was being fed on the milk from these cows was itself well, but lost all of its eight-weeks-old kittens, five in number, during the outbreak in the family. A dog receiving milk from the same cattle showed signs of illness and was noticed to vomit repeatedly."

This case does not entirely agree with the claim quite commonly advanced in "milksick" sections in the State to the effect that so long as cows are being milked or their calves are suckling, they show no signs of trembles. The calves, however, may sicken and die or persons who use the milk may be affected with milksickness. In due time, however, the milk is suspected and in consequence, the cows are left to go dry and then develop the disease. This peculiarity furthermore finds support in the writings of Drake (1841), Graff (1841), and Kimmel (1891). It is further strengthened by the common observation among farmers that in the herd of cows, heifers, and steers, the heifers and steers become affected earlier than cows in lactation.

To Lambs.—Experiment 22.—The present experiments bearing upon the acquisition of milksickness through the milk deal with suckling lambs whose mothers were fed white snakeroot as previously recorded in Table III. The mothers of the lambs, the data on which lambs are recorded in Table VI, were also well advanced in the period of lactation as were those reported in Table IV. This fact is believed to be the potent factor in determining the small number of cases of milksickness which developed.

TABLE VI—RESULTS OF TRANSMISSION OF THE DISEASE THROUGH THE MILK FROM EWES TO LAMBS. EXPERIMENT 22.

Animal No.								*Feed given.*	
Ewe No.	*Lamb No.*	*Initial weight. Lbs.*	*Experiment begun*	*Date of death.*	*No. days on experiment.*	*Weight at death. Lbs.*	*Gain or loss. Lbs.*	*Grain. Lbs.*	*Kale. Lbs.*
171	244	38	May 13	June 17	35	27.5	—10.5	9	33
162	243	50	May 13	July 25*	73	61	11	30	71
175	242	40	May 13	June 17	35	39	—1	15	32
167	241	33	May 13	July 25*	73	32	—15	36	71
12	237	46	May 13	July 25*	73	56	10	35	71
168	200	48	May 13	July 15*	83	45	—3	35	60

*These lambs were put on pasture on the dates indicated.

Two lambs, Nos. 244 and 242, developed genuine cases of milksickness and died thirty-five days after the experiment was begun, June 17. Ewe 171, the mother of lamb 244, showed no evidence of trembles until a few days before her death, which occurred, as noted before, on August 30. These individuals are shown in Fig. G, at a time when the lamb had passed into a state of coma. The mother of lamb 244 never manifested any evidence of trembles although she was continued on the experiment until September 2. This fact accords with the observation which has previously been made by Jordan and Harris (1909) that animals can transmit the disease through the milk without themselves ever manifesting any signs of the disorder.

Lambs 237 and 241 were employed after this experiment was concluded in tests on the toxicity of expressed sap as has been reported in Experiment 21. The other two lambs, Nos. 243 and 200, were placed on pasture.

The butter from cows affected with trembles is also generally believed to be the source of milksickness. A number of publications dealing with this phase of the subject have appeared in which the authors, among whom are Johnson (1866), Gray (1881), Beach (1883), Scott (1889), Beck (1905), and Jordan and Harris (1909), commit themselves to this belief. The last named writers describe an outbreak which came under their observation at Morris, Ill., in 1908. Five cases developed in a family which secured butter from a farm six miles distant. The cows which gave the milk from which this butter was made, ranged in woodland in which eight cattle had contracted trembles two years earlier. About a month after the recovery of these five persons, a typical case appeared in one of the young men on the farm from which the butter had been procured. In concluding this account, they state that "There seems little doubt, therefore, in view of all the facts, that butter brought from the 'milksick' farm was responsible for the cases."

To Mice.—Experiment 23.—Opportunity has not been afforded in the present experimental study to secure conclusive data upon butter as an agency in the transmission of milksickness. Three mice were fed butter made from the milk of a cow feeding upon white snakeroot. One died about two weeks after feeding was begun, another a week later, while the other one remained unaffected. Aside from general debility, no other symptom was prominent in these two animals, and the cause of their death could not be determined with certainty. It is reasonable to conclude, however, in the light of experiments on milk as a carrier of milksickness, that the disease may be transmitted through butter.

No clear-cut evidence pointing to a relationship between cheese and the development of the disease appears in available medical literature. Some few writers (Scott, 1889) assume that it is a generally accepted fact and in view of the evidence that milk and butter are capable of transmitting the disease, it is logical to suppose that cheese may also be a carrier. No feeding tests, however, have ever been directed toward the settlement of this claim.

b. Through the Agency of Meat

Numerous records exist of the transmission of this disease through the eating of flesh of animals affected with trembles. Coleman (1822), Lewis (1829), Sale (1891), and Conner (1904) cite specific instances of the acquisition, by man, of this disease from meat. Yandell (1867) has included in his account statements which are contrary to this idea. Statements apparently from eye-witnesses (Coleman, 1822; De Bruler, 1858) have, moreover, been made to the effect that carnivorous animals may acquire the disease from the flesh of animals dead of trembles. More remarkable than this, however, is the statement that these animals can transmit the disease to others indefinitely. Instances like the following from McCall's (1830) report illustrate the point in question. Some sheep which died of trembles were eaten by hogs, which in turn, succumbed to the same disease. The carcasses of all of the hogs except one were burned. Chickens which ate of this one were eaten in turn by persons who subsequently developed cases of milksickness. Another similar record by De Bruler (1858) states that a cow gave the disease to her calf, whose body was eaten by dogs. The dogs in turn died of trembles and a pet crow which fed on the dogs' flesh also died.

The more recent experiments by Jordan and Harris (1909) in which four dogs were fed upon flesh of animals dead of trembles resulted in the production of no ill effects.

To Dogs.—Experiment 24.—These results with meat are in accord with the results secured in the present studies. During 1916, the car-

casses, including livers, hearts, kidneys, and spleens of three sheep dead of trembles were fed to three dogs with no resultant ill effects. During the next season, four dogs were given the bodies of eight animals with no manifestation of trembles. It can only be suggested with reference to the observations of others to the effect that carnivorous animals may die after having eaten the flesh of an animal dead of trembles, that ptomaines may have been present as the result of bacterial growth. This was guarded against in the present experiments by placing the carcasses, immediately after the autopsies had been performed, in a refrigerator. Daily portions were then given sufficient to satisfy the dogs' hunger.

Summary of Feeding Experiments.

During the course of the feeding experiments with white snakeroot, a total of 41 sheep and lambs have been subjected to experimental conditions. Three others died in the experimental work with sodium compounds, to be reported later in this paper. Twenty-eight of these died and all except two were observed to have been characteristically affected with trembles or milksickness. These two were infested with stomach worms, which infestation may have been a contributory cause of their death. Two lambs contracted milksickness from the milk of ewes feeding upon white snakeroot.

Two hogs were fed white snakeroot. One of these animals contracted a fatal case of trembles and the other remained apparently unaffected.

Twenty-nine guinea pigs, fifteen of which succumbed on the experiments, were given white snakeroot or some of the products prepared from this plant.

Seven dogs ate of the flesh of sheep dead of trembles with manifestly no ill effects.

Three mice were given butter from the milk of a cow feeding upon white snakeroot. Two of them died while the other remained unaffected.

Post-Mortem Examinations

No detailed studies of the pathological anatomy of animals dead of trembles or milksickness, other than those of Jordan and Harris (1909) appear in the voluminous literature on this disease. These authors give a general historical account of autopsies by other writers. These accounts give the impression of being fragmentary and indicate a lack of familiarity with anatomy in general and of experience with making post-mortem examinations. Such statements as the following indicate the point in question.

Bennett (1822) says that the stomach contents of cattle is dry and that the liver has a morbid appearance. Beck (1822) describes the heart and aorta as greatly enlarged and their inner coat sloughy. Mil-

ler (1867) asserts that gastric and hepatic lesions accompany the disease. Hibberd (1844) mentions the finding of a diminution of the caliber of the stomach and intestine in all of the cases examined. Mendenhall (1861) describes the inner coat of the stomach and intestine as being gangrenous. Newman (1867) records the singular observation that "in examining a milk cow after death the skin was found very much thickened and covered with small pustules." Dicky (1852) states that the peritoneum and small intestine showed signs of inflammation. Graff (1841) says that there is evidence of cerebral inflammation, of a similar condition of the stomach and small intestines, that the spleen is enlarged and the liver softened. Way (1893) noted congestion of the cerebral meninges in the case of a six-weeks-old calf.

Jordan and Harris (1909) had opportunity to perform autopsies upon several cattle, two lambs, and one horse. The following account of the microscopical appearance of these animals covers their findings. Externally the body presents nothing on inspection that is worthy of note. There may be present in the pleural cavities a small quantity of clear, yellow fluid. On opening the thoracic cavity, the lungs do not collapse. A quantity of frothy fluid exudes from the sectioned surface of the lungs. As a rule, the pericardial sac contains varying quantities of clear, straw-colored fluid which coagulates when exposed to the air. Numerous ecchymotic areas which are more numerous at the base of the heart, occur along the course of the cardiac veins. There was noted on section of the heart either fatty areas or streaks, or cloudy swelling.

The peritoneal cavity contains no abnormal amount of serous fluid. The liver is uniformly enlarged and of a purple color, being full of blood. The consistency of the liver substance is soft and friable, and of the "nutmeg" appearance. Blood drips freely from the sectioned surface. The parenchymatous tissue is fatty. The kidneys are always enlarged and engorged with blood. Cloudy swelling of the parenchyma and in some cases slight fatty changes are noted. The bladder may be injected. In some cases, the urine is cloudy and apparently contains blood. The mucosa of the small intestines may show injection and ecchymoses. The meningeal vessels of the brain appear congested.

In the microscopical examination, these authors find that the most profound pathological changes occur in the heart, liver, and kidneys. In the heart there may be noted cloudy swelling and fatty changes. In the liver the parenchymatous cells appear swollen with more or less cloudy swelling and fatty metamorphoses. The central veins are distended with blood. The kidneys show hyperemia, glomerulitis, and parenchymatous degeneration.

The following is a detailed report of seven representative cases in sheep and lambs.

CLINICAL DATA ON CASE 1, TABLE VII, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF EWE 168.

	Temperature.			Pulse.			Respiration.			Atmospheric Temperature.			Character of Day
Date.	A. M.	M.	P. M.	A. M.	M.	P. M.	A. M.	M.	P. M.	Max.	Min.	Mean	
5–11	.....	.....	103.6	.....	.....	63	.....	.....	30	70	47	58	Cloudy.
5–12	.....	.....	103.8	.....	.....	60	.....	.....	42	61	46	54	Partly cloudy.
5–13	.....	102.1	.....	.....	60	.....	.....	48	.....	60	42	51	Partly cloudy.
5–14	102.1	101.2	102.0	66	69	54	48	43	30	66	43	54	Partly cloudy.
5–15	101.4	101.3	103.5	60	54	66	42	36	48	76	49	62	Clear.
5–16	102.0	102.0	101.9	60	66	66	45	42	48	80	57	68	Cloudy.
5–17	101.7	101.9	102.1	60	63	66	30	45	48	85	62	74	Clear.
5–18	101.4	102.0	102.2	63	60	60	36	39	45	87	65	76	Clear.
5–19	101.8	101.6	102.6	69	66	66	42	48	54	92	64	78	Clear.
5–20	101.6	102.1	102.6	54	60	66	36	54	57	90	65	78	Clear.
5–21	101.6	102.0	102.7	72	75	72	33	42	60	90	64	77	Clear.
5–22	102.1	102.2	102.7	66	54	60	42	42	66	88	62	75	Clear.
5–23	101.5	102.8	102.8	54	66	60	30	42	42	76	55	66	Partly cloudy.
5–24	100.6	101.6	102.6	60	63	60	27	33	33	72	49	60	Clear.
5–25	101.4	101.0	102.2	66	69	69	27	33	36	77	55	66	Partly cloudy.
5–26	101.2	102.0	102.6	57	60	72	30	30	36	77	53	65	Partly cloudy.
5–27	101.7	102.0	102.6	66	72	63	27	42	36	86	64	75	Cloudy.
5–28	101.7	101.3	102.6	66	57	60	30	30	42	80	68	74	Cloudy.
5–29	101.4	.....	101.8	66	.....	60	48	.....	36	78	59	68	Clear.
5–30	101.3	101.6	101.5	60	60	66	30	36	42	82	55	68	Clear.
5–31	101.8	102.4	101.5	66	66	60	36	36	30	78	59	68	Cloudy.
6–1	101.3	103.0	102.8	66	66	63	36	42	54	89	66	78	Partly cloudy.
6–2	102.0	102.4	103.3	75	66	69	42	48	54	90	65	78	Clear.
6–3	102.2	102.6	103.4	69	57	66	48	72	60	91	66	78	Partly cloudy.
6–4	101.8	102.4	102.6	66	69	72	36	36	42	73	64	68	Cloudy.
6–5	101.9	101.9	102.4	66	69	78	36	33	42	85	64	74	Partly cloudy.
6–6	102.2	102.0	103.0	72	72	66	36	42	54	89	67	78	Partly cloudy.
6–7	101.8	102.3	103.0	60	66	63	30	45	54	84	70	77	Partly cloudy.
6–8	102.0	102.8	102.6	66	66	63	36	39	36	86	64	75	Partly cloudy.
6–9	101.6	102.0	102.2	72	63	59	42	66	54	86	64	75	Partly cloudy.
6–10	101.6	101.4	101.5	66	66	63	30	30	27	76	64	70	Cloudy.
6–11	101.2	101.5	102.2	63	66	66	33	33	30	83	65	74	Partly cloudy.
6–12	101.4	102.2	102.8	75	60	57	36	30	54	88	67	78	Clear.
6–13	101.6	101.4	102.2	78	57	60	39	30	48	88	68	78	Partly cloudy.
6–14	101.5	101.8	102.0	63	60	66	27	36	27	84	68	74	Cloudy.
6–15	100.7	102.2	102.4	68	60	57	33	30	27	78	62	70	Partly cloudy.
6–16	101.6	101.2	101.6	60	57	57	30	36	27	73	56	64	Clear.
6–17	99.6	100.3	101.8	60	63	63	42	36	36	76	54	65	Clear.
6–18	100.5	101.2	102.0	66	72	57	42	30	39	82	58	70	Clear.
6–19	100.8	101.2	101.8	51	54	60	36	30	45	80	60	70	Cloudy.
6–20	101.8	102.0	102.4	60	60	63	36	39	66	85	63	74	Clear.
6–21	101.4	102.2	102.4	60	66	60	48	42	66	88	64	76	Partly cloudy.
6–22	100.8	101.0	101.6	66	66	63	30	48	54	85	63	74	Clear.
6–23	101.8	102.2	102.4	54	60	63	24	54	60	91	69	80	Clear.
6–24	102.0	103.0	103.5	66	72	60	48	84	72	93	67	80	Clear.
6–25	102.1	102.6	103.3	66	75	60	48	81	84	88	68	78	Clear.
6–26	101.6	102.0	103.5	72	72	66	57	72	90	91	72	82	Partly cloudy.
6–27	102.6	102.2	103.4	72	69	66	60	84	96	92	71	82	Clear.
6–28	102.0	102.4	102.6	75	66	69	54	72	84	90	69	80	Partly cloudy.
6–29	101.6	101.8	102.4	72	66	69	48	60	48	86	67	76	Cloudy.
6–30	102.2	101.8	102.6	66	63	63	36	54	54	84	65	74	Partly cloudy.
7–1	101.8	102.2	102.5	60	60	57	48	48	63	87	67	77	Clear.
7–2	102.0	102.2	102.9	60	66	63	33	54	54	88	67	78	Partly cloudy.
7–3	102.2	101.8	102.3	60	63	60	36	45	66	85	67	76	Cloudy.
7–4	102.2	102.0	102.1	60	60	63	39	54	36	79	65	72	Cloudy.
7–5	101.9	102.2	103.0	60	66	69	51	66	66	85	63	74	Partly cloudy.
7–6	102.0	102.3	102.0	60	66	63	48	57	48	83	69	76	Partly cloudy.
7–7	102.0	102.6	102.8	63	66	66	42	42	36	81	69	75	Cloudy.
7–8	102.0	101.8	101.8	54	66	60	36	60	48	86	68	78	Partly cloudy.
7–9	102.3	101.9	102.6	72	63	66	42	48	72	89	70	70	Clear.
7–10	102.2	102.6	103.0	66	63	60	48	48	54	88	67	78	Partly cloudy.
7–11	102.2	103.2	102.7	51	54	60	36	48	42	83	66	74	Clear.
7–12	102.4	102.5	102.4	57	60	66	42	54	54	92	67	80	Partly cloudy.
7–13	101.6	101.6	102.2	63	66	72	30	36	57	86	67	76	Partly cloudy.
7–14	101.4	101.5	102.4	75	72	78	42	48	48	86	67	76	Partly cloudy.
7–15	104.2	Died	.....	69	.....	.....	42	.....	.....	90	69	80	Clear.
7–16	.....	.....	.....	.....	.....	.....	.....	.....	.....	91	69	80	Clear.
7–17	.....	.....	.....	.....	.....	.....	.....	.....	.....	90	67	78	Partly cloudy.
7–18	.....	.....	.....	.....	.....	.....	.....	.....	.....	82	66	74	Cloudy.
7–19	.....	.....	.....	.....	.....	.....	.....	.....	.....	78	66	72	Cloudy.
7–20	.....	.....	.....	.....	.....	.....	.....	.....	.....	79	68	74	Cloudy.
7–21	.....	.....	.....	.....	.....	.....	.....	.....	.....	80	69	74	Cloudy.
7–22	.....	.....	.....	.....	.....	.....	.....	.....	.....	86	71	78	Partly cloudy.
7–23	.....	.....	.....	.....	.....	.....	.....	.....	.....	89	72	80	Partly cloudy.

These data show that in ewe 168 there were no marked abnormalities in temperature, pulse, and respiration. There has been included with this table a statement of the meteoric conditions since they exert an influence upon the temperature, pulse, and respiration of animals.

Clinical Notes. The first symptoms appeared July 13, when the respiration was slightly jerky. On the 14th, she lay with head and neck extended and jaw resting upon the ground. After standing for about a half-minute, she would begin to tremble as noted in all the other cases. As soon as trembling began, she would lie down. In the afternoon the symptoms were more aggravated. She went into a state of coma during the night before she died, and death occurred July 15, at about 8 A. M.

Blood Study. On May 18 a study was made of the blood of ewe 168 to determine the normal condition prior to the feeding of white snakeroot. The following is the result of this study:

Numerical count:	
Erythrocytes	8,040,000
Leucocytes	14,000
Differential count:	
Neutrophiles	46 per cent
Lymphocytes, large	4 per cent
Lymphocytes, small	45 per cent
Eosinophiles	2 per cent
Mast cells	3 per cent
Hemaglobin	72 per cent

On July 14 a study of the blood was made with the following result:

Numerical court:	
Erythrocytes	9,540,000
Leucocytes	9,000
Differential count:	
Neutrophiles	45 per cent
Lymphocytes, large	14 per cent
Lymphocytes, small	39 per cent
Mast cells	2 per cent
Hemaglobin	72 per cent

There was thus a slight increase in the small lymphocytes at the expense of the large lymphocytes, a slight increase in the erythrocytes, and a numerical decrease in the leucocytes. The hemaglobin remained normal.

Protocol. Externally the body presents nothing worthy of note.

The Thoracic Cavity.—The lungs appear normal and collapse when the thorax is opened. There is neither pneumonia, broncho-pneumonia, nor pleuritis. The color of the lung is pale salmon. No excess of fluid is found in the thoracic cavity.

The Heart.— There is an excessive amount of pericardial fluid. Petechiation of the epicardium in the region of the coronary arteries and at the base of the heart is noted. The heart is filled with dark, coagulated blood. There are no agony thrombi and the muscles appear pale in color.

The Abdominal Cavity.—An excessive amount of serous fluid exists in the abdominal cavity. Muco-enteritis involving the abomasum and duodenum and a portion of the jejunum is present. Stomach worms are found in the abomasum. The small and large intestines are affected with nodular disease. The large intestines otherwise appear normal.

The Liver.—The liver weighs one pound thirteen and one-half ounces. It is of a dark metallic color and is congested so that blood drips from the sectioned surface. The gall bladder is filled with a rather dark, tarry bile. Cloudy swelling is evidently present.

The Kidneys.—Both kidneys weigh four and one-half ounces. Externally they present a metallic color. Both active and passive congestion and cloudy swelling are present. The glomerules can be noted as minute, red pin point-like spots in the renal cortex.

The Bladder.—Empty and apparently normal.

The Musculature.—Normal.

The Brain.—Congested.

The Lympth Glands.—Normal.

Microscopical Examination. *The Liver.*—Both active and passive congestion, cloudy swelling and fatty degeneration are noted.

The Kidneys.—Both active and passive congestion are present. Glomerulitis is noted and some of the convoluted tubules show evidence of fatty degeneration.

The Brain.—The blood vessels are congested. An occasional polymorphonuclear leucocyte and plasma cells occur throughout the tissues. The brain cells are not shrunken and appear normal.

The heart.—The heart muscle fibers have lost their cross striation and many areas show fatty degeneration. The nuclei stain deeply, in fact, may be considered picnotic. The blood vessels are congested:

The Lungs.—Normal.

The Lymph Glands.—Normal.

The Pancreas.—Normal.

The Adrenal Glands.—Normal.

The Duodenum.—The duodenum is infiltrated with round cells.

The Blood Vessels.—Congested.

CASE 2, TABLE VIII, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF LAMB 200.

	Temperature.			*Pulse.*			*Respiration.*		
Date.	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*
5–11	.....	.....	103.1	80	....	80	.....	.....	112
5–12	.....	.....	104.0	....	....	72	.....	.....	96
5–13	.....	103.2	.....	....	72	....	79	.....	.....
5–14	103.2	.....	102.8	78	86	72	72	87	54
5–15	102.9	102.9	103.1	78	90	84	66	108	90
5–16	103.3	102.9	103.3	84	84	79	90	120	114
5–17	103.7	103.6	103.4	78	84	78	126	120	132
5–18	103.6	103.2	103.0	84	96	88	132	126	132
5–19	104.0	104.0	103.4	78	78	78	126	142	132
5–20	103.6	103.7	103.9	84	84	78	139	156	156
5–21	103.8	103.0	103.9	78	84	87	138	144	158
5–22	104.0	103.4	103.4	84	78	84	114	114	132
5–23	103.6	103.8	103.7	84	84	84	138	144	147
5–24	103.2	103.2	103.2	84	84	78	78	90	102
5–25	103.0	103.0	103.4	72	78	84	90	96	108
5–26	103.2	103.0	103.1	87	84	84	90	78	138
5–27	103.8	103.6	103.4	84	72	72	108	114	102
5–28	103.2	103.6	103.8	72	66	72	72	90	108
5–29	103.0	.....	103.9	81	....	78	72	.....	90
5–30	102.7	103.0	103.7	72	84	72	60	108	78
5–31	103.0	103.1	103.7	69	72	78	66	84	90
6– 1	104.0	103.9	103.9	84	69	72	120	126	108
6– 2	103.0	103.3	103.4	78	69	72	108	126	138
6– 3	104.0	104.0	103.9	72	81	72	120	114	126
6– 4	103.0	103.7	103.8	75	84	84	84	96	120
6– 5	103.2	103.6	103.7	78	84	81	105	102	102
6– 6	103.2	103.6	103.9	75	72	87	114	102	108

Date.	Temperature. A.M.	M.	P.M.	Pulse. A.M.	M.	P.M.	Respiration. A.M.	M.	P.M.
6– 7	103.4	103.7	104.2	72	75	81	108	108	102
6– 8	103.9	104.0	103.8	84	75	90	96	108	126
6– 9	102.8	103.0	103.2	72	84	75	84	90	78
6–10	103.3	103.8	103.7	72	84	84	54	87	90
6–11	103.4	103.8	103.8	78	87	81	96	114	114
6–12	103.4	103.8	103.8	81	78	82	114	120	132
6–13	103.8	104.2	104.2	72	72	75	96	96	120
6–14	104.3	104.1	103.8	81	75	60	114	120	102
6–15	103.1	104.0	104.7	72	66	66	66	90	96
6–16	102.8	103.3	104.0	78	72	60	90	60	60
6–17	102.4	103.5	104.2	60	60	54	72	66	60
6–18	103.3	103.0	103.0	63	60	60	84	90	102
6–19	103.2	103.5	103.8	60	57	66	54	72	78
6–20	103.1	104.1	104.2	72	60	72	90	90	96
6–21	103.4	104.2	104.2	69	75	63	102	90	96
6–22	103.4	103.4	104.1	72	69	78	78	108	78
6–23	103.9	104.5	104.0	69	72	75	60	90	108
6–24	104.0	104.1	104.0	72	78	72	90	120	114
6–25	103.7	103.4	104.0	60	72	69	90	90	108
6–26	103.5	104.0	104.2	69	66	66	96	90	120
6–27	103.6	104.0	104.4	69	72	60	120	120	102
6–28	102.9	104.0	103.9	63	61	68	60	108	114
6–29	104.2	103.6	104.0	66	72	60	90	96	78
6–30	103.1	103.5	103.5	66	72	72	54	90	96
7– 1	103.6	103.6	104.0	54	66	57	66	90	78
7– 2	103.6	104.2	104.0	60	72	60	78	96	96
7– 3	103.8	103.4	103.4	60	69	54	54	75	36
7– 4	103.2	103.4	103.9	66	60	60	66	48	72
7– 5	103.4	103.4	103.8	54	66	69	48	78	108
7– 6	103.2	103.6	103.5	66	66	72	66	84	90
7– 7	103.4	103.8	103.7	72	72	66	90	84	90
7– 8	103.2	103.9	103.8	54	57	60	48	84	108
7– 9	103.2	103.6	103.6	57	51	57	66	66	90
7–10	103.7	104.0	104.1	63	60	66	84	108	144
7–11	103.1	103.0	104.0	60	54	54	36	48	72
7–12	103.5	103.9	104.3	60	60	66	78	78	90
7–13	103.3	103.8	104.1	66	66	69	73	72	90
7–14	103.2	103.7	104.6	54	60	69	66	84	84
7–15	103.5	103.5	103.8	60	63	60	66	84	96
7–16	103.4	104.1	104.0	60	66	60	78	90	96
7–17	103.8	103.9	103.9	66	60	72	108	72	84
7–18	103.8	104.0	103.0	66	66	69	54	84	78
7–19	103.4	104.0	103.4	69	63	66	72	84	78
7–20	104.7	103.8	103.6	72	69	60	90	72	72
7–21	103.8	104.4	103.8	66	63	69	102	90	84
7–22	103.9	103.9	103.5	66	69	66	96	102	108
7–23	104.2	104.3	103.7	57	60	66	102	78	168
7–24	103.9	103.8	103.6	60	66	66	84	114	108
7–25	103.7	104.0	103.8	69	69	72	90	96	90
7–26	103.8	103.9	103.6	66	66	72	108	114	102
7–27	103.8	104.2	104.0	60	72	72	102	114	114
7–28	104.4	103.8	104.4	72	75	78	102	102	120
7–29	103.9	104.2	104.3	69	72	72	84	114	114
7–30	105.0	104.7	104.8	69	72	66	108	114	132
7–31	104.9	105.0	105.1	72	66	72	108	114	120
8– 1	104.7	104.8	105.0	69	72	69	120	126	120
8– 2	104.7	104.8	105.1	72	69	72	120	114	120
8– 3	103.8	103.9	104.4	78	84	81	66	108	108
									Died

These data show a slight disturbance in temperature and pulse and a very considerable increase in respiration.

Clinical Notes. The feed consisted of one-half pound of oats and one-fourth pound of weeds given twice daily and one pound of kale at noon. Feeding was begun July 16, and during this experiment this animal received 17 pounds of oats, 8.7 pounds of white snakeroot, and 17 pounds of kale. The first symptoms were noted August 1, when she appeared to be sluggish, with loss of appetite. On August 3 she ate sparingly. After standing about three-quarters of a minute she began to tremble and would soon lie down. Respirations were accompanied by groaning. At noon, the trembling was more violent than in the morning and she could not remain standing as long. During the afternoon she lay with neck outstretched and jaw resting upon the ground. She was found dead the next morning.

Blood Study. On May 18 a study was made of the blood to determine its normal condition. The following are the results:

Numerical count:	
Erythrocytes	13,760,000
Leucocytes	11,000
Differential count:	
Neutrophiles	19 per cent
Lymphocytes, large	5 per cent
Lymphocytes, small	72 per cent
Eosinophiles	4 per cent
Hemaglobin	77 per cent

On August 3, after severe symptoms had developed, another study was made. The results are as follows:

Numerical count:	
Erythrocytes	15,520,000
Leucocytes	7,000
Differential count:	
Neutrophiles	59 per cent
Lymphocytes, large	13 per cent
Lymphocytes, small	28 per cent
Hemaglobin	78 per cent

There was an apparent increase in the erythrocytes and an increase in neutrophiles at the expense of lymphocytes. There was a marked decrease in the total number of leucocytes. The decrease may have been in the lymphocytes, in which case there would be an apparent increase in the neutrophiles over the lymphocytes. The eosinophiles have entirely disappeared. The hemaglobin remains the same.

Urine Study. A study of the urine was made after severe symptoms of trembling had developed. The following is the result:

Physical examination:
- Color—Light port wine.
- Specific gravity—1015.

Chemical examination:
- Reaction—Neutral.
- Albumin—Present.
- Sugar—None.
- Carbonates—Present.
- Sulphates—Present.
- Phosphates—Present.
- Chlorides—Present.
- Hemaglobin—None.

Microscopic examination:
- Granular tube casts—Present.
- Epithelia—
  - Circular cells.
  - Spindle cells.
  - Squamous cells.

Albuminuria is present and the color indicates that hemaglobin may be present; however, Heller's test for the same was negative. She was normally

eliminating her chlorides, carbonates, phosphates, and sulphates. Tube casts of a granular type are present.

Protocol. There is a discharge from the nostrils indicating that vomiting might have taken place. Otherwise the body presents nothing on inspection that is to be considered worthy of note. There is no conjunctivitis. The lymph glands are not palpable, and there are no cutaneous and subcutaneous lesions.

The Thoracic Cavity.—There is evidence of neither pleuritis, pneumonia, nor bronchitis. The lungs do not collapse when the thorax is opened. The sectioned surface of the lungs shows a frothy, bloody material. The lungs are congested. No ecchymoses are found on the serous surfaces of the pleura or pericardium.

The Heart.—The pericardium appears normal, and there is no evidence of endocarditis. The left side of the heart is filled with dark, coagulated blood. There is no antemortem clot. The heart muscles appear pale.

The Abdominal Cavity.—The quantity of fluid in the abdominal cavity is normal. There is no peritonitis and both small and large intestines appear normal. The abomasum and duodenum are injected and the mucosa shows evidence of muco-enteritis. No stomach worms are present.

The Spleen is normal.

The Lymph Glands are normal.

The Musculature is normal.

The Brain appears somewhat congested.

The Bladder is filled with urine.

The Liver.—The liver appears dark and congested. When cut, the blood drips from the sectioned surface.

The Kidneys.—The capsules present a metallic appearance. The kidneys appear swollen and their capsules, which are easily separable, are tense. Both active and passive congestion are noted. The glomerules can be recognized as minute red, pin-point-like spots prominent throughout the cortical portion of the kidneys. The grayish appearance of the parenchyma gives evidence of cloudy swelling.

Cultural Examination.—Two cultures on glycerine agar and plain agar from both the liver and kidney were made with negative results.

Blood smears with Romanowsky's stain were negative. Smears made from the liver substance and stained with fuchsin were likewise negative.

Microscopical Examination. *The Liver.*—Sections of the liver show advanced fatty degenerative changes. They also present the appearance of both active and passive congestion and cloudy swelling.

The Kidneys—Both active and passive congestion and glomerulitis are present. The glomerules are congested and shrunken, leaving a space between the glomerule and the capsule of Bowman (Fig. N). Cloudy swelling is present (Fig. M). In some areas the lumina of the convoluted tubules are obliterated, the cells being swollen and pushed out toward the center. Cytoplasm is granular and many of the cells have lost their nuclei.

The Lungs.—The lungs are congested and there is an occasional air cell in which are noted a few erythrocytes and polymorphonuclear leucocytes.

The Brain.—The vessels of the brain are congested. An occasional plasma cell occurs throughout the tissues. Some areas show cellular invasion, the

kind of cell being mostly of the small round type. The brain cells appear normal.

The Pancreas is normal.

The Adrenal Glands are normal.

The Heart muscle shows some fatty degeneration and in these areas the muscle fibers have lost their cross-striation.

CASE 3, TABLE IX, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF LAMB 241.

	Temperature.			*Pulse.*			*Respiration.*		
Date.	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*
5-11	.....	.....	104.1	....	....	82	.....	.....	74
5-12	.....	.....	104.0	....	....	66	.....	.....	70
5-13	.....	104.0	.....	....	63	....	.....	71	.....
5-14	103.1	103.0	103.2	80	84	72	78	80	48
5-15	102.9	103.1	103.0	78	120	84	57	108	114
5-16	102.5	102.6	103.2	72	72	84	84	96	108
5-17	103.7	103.9	103.0	96	88	88	168	172	150
5-18	103.7	102.2	102.5	90	84	84	150	114	118
5-19	103.6	103.2	103.6	72	70	78	156	168	190
5-20	103.5	103.0	102.7	84	84	80	180	190	186
5-21	103.1	102.5	103.8	96	90	84	186	162	168
5-22	103.4	103.7	103.6	84	78	78	178	156	178
5-23	103.9	103.7	103.3	84	90	84	129	126	156
5-24	102.8	103.2	103.2	84	78	84	120	120	108
5-25	103.0	103.0	102.4	84	78	72	126	96	144
5-26	103.4	103.8	103.7	90	87	84	102	132	120
5-27	103.3	103.2	103.7	75	84	72	96	150	156
5-28	103.8	103.3	103.5	72	84	84	144	138	132
5-29	102.8	.....	102.6	84	....	84	54	.....	84
5-30	102.8	103.0	103.0	72	78	84	102	114	114
5-31	103.0	103.2	103.0	84	87	75	88	62	108
6- 1	103.0	103.2	103.0	78	78	78	132	144	126
6- 2	103.1	103.4	103.0	75	81	90	138	108	132
6- 3	103.2	103.5	103.5	78	75	72	156	138	78
6- 4	103.1	104.0	103.5	75	84	87	90	86	102
6- 5	103.0	103.0	103.3	75	84	72	66	96	72
6- 6	103.4	103.6	104.0	87	75	75	126	102	108
6- 7	103.7	103.6	104.1	75	78	69	48	102	90
6- 8	104.1	104.2	103.7	78	75	78	90	102	60
6- 9	103.2	103.8	103.6	72	72	75	54	48	84
6-10	103.2	103.2	103.5	81	78	84	60	84	78
6-11	102.8	103.6	104.2	72	78	75	54	96	120*
6-12	104.9	105.2	105.4	84	84	90	102	132	154
6-13	105.6	103.7	105.7	72	84	90	120	120	126
6-14	106.2	106.2	106.0	75	78	87	144	120	66
6-15	106.3	105.4	105.7	78	72	78	60	78	66
6-16	105.9	105.9	105.6	72	81	78	54	54	60
6-17	106.0	105.4	105.4	84	78	75	96	108	78
6-18	105.9	105.1	105.4	72	90	72	66	132	96
6-19	104.8	104.6	104.4	78	81	75	72	120	72
6-20	105.0	104.8	104.4	84	72	84	66	138	102
6-21	104.2	105.1	104.8	78	78	75	66	138	108
6-22	104.4	104.7	104.4	69	72	78	54	108	60
6-23	104.3	104.7	104.6	78	78	81	114	80	80
6-24	103.6	104.3	104.0	75	84	75	60	108	126
6-25	103.8	103.7	104.6	81	72	78	102	66	132
6-26	104.2	104.5	104.8	78	75	84	102	60	108
6-27	103.4	103.8	104.0	78	75	72	96	102	84
6-28	103.2	103.6	104.2	69	66	72	36	120	126
6-29	103.8	103.4	103.9	78	75	72	96	90	60
6-30	103.7	103.3	103.5	72	54	66	54	60	42
7- 1	103.2	103.2	103.6	72	72	69	48	96	54
7- 2	103.6	103.6	103.6	78	78	66	72	84	48
7- 3	103.4	103.6	103.8	63	60	60	48	54	66
7- 4	102.9	103.3	103.5	66	72	75	42	84	54
7- 5	103.4	103.5	103.8	78	72	69	81	78	66
7- 6	103.8	103.6	103.0	78	72	69	114	66	84
7- 7	103.2	103.4	103.6	72	72	66	42	78	60
7- 8	103.3	103.4	103.4	66	66	66	60	90	72
7- 9	103.8	103.3	103.4	63	66	66	66	72	96
7-10	103.2	103.2	103.7	72	72	75	84	66	84
7-11	103.4	103.5	103.4	69	72	66	60	54	69
7-12	103.5	103.4	104.2	72	72	66	48	84	66

*Docked.

Date.	Temperature. A.M.	M.	P.M.	Pulse. A.M.	M.	P.M.	Respiration. A.M.	M.	P.M.
7–13	104.3	103.8	103.9	66	66	72	72	72	60
7–14	103.4	103.6	104.0	66	69	75	48	48	84
7–15	103.3	103.0	103.5	66	66	60	42	78	66
7–16	103.3	103.0	103.9	66	66	66	48	54	96
7–17	103.3	103.4	103.3	66	72	72	72	90	66
7–18	102.3	103.0	102.8	66	60	66	42	48	60
7–19	103.0	103.0	102.5	60	60	57	54	48	36
7–20	102.6	102.3	103.0	63	57	54	42	48	54
7–21	102.4	102.7	103.0	60	60	60	42	54	54
7–22	103.4	103.3	102.8	66	63	66	66	42	66
7–23	103.4	103.8	103.3	66	66	63	42	54	48

This suckling lamb was unfortunately docked June 11, which accounts for the increased temperature, pulse, and respiration on that and several succeeding days.

Clinical Notes. The animal was put into the pen July 30, and was given 250 c.c. of expressed juice at 2:30 P. M. He refused supper and stood in a drooping posture. Next morning he ate about one-fourth pound of oats and was given another 250 c.c. of juice. In the evening, a third quantity of 250 c.c. of juice was given. He refused to eat in the afternoon. On August 1, breathing was accelerated and was accompanied by groaning. He refused all feed. He refused feed on the following day, gritted his teeth, breathing was jerky, and he appeared droopy. On August 3 he ate about one-fourth pound of oats and was more active, the symptoms having apparently subsided. He was given 250 c.c. of juice in the afternoon. On August 4 he refused the morning feed and 250 c.c. of juice were given. He ate all feed in the afternoon and was given another 250 c.c. of juice. On August 5 two doses of 250 c.c. each of juice were administered. A slight trembling was apparent on the morning of August 6 and he could stand without difficulty. No signs of trembling were noted in the afternoon, but he stood with head down and back bowed. He ate with normal appetite. Trembling was marked and no food was taken on August 7. In the afternoon the symptoms were more aggravated. A state of coma had set in during the following night, and on August 8 respirations were accelerated. This animal was killed on the morning of the 9th, having been in a state of coma since the night of the 7th.

Blood Study. On May 18 a blood study was made to determine the normal condition of the blood of this lamb prior to the commencement of the feeding test with white snakeroot. The following is the result:

Numerical count:

Erythrocytes	13,440,000
Leucocytes	10,000

Differential count:

Neutrophiles	27 per cent
Lymphocytes, large	5 per cent
Lymphocytes, small	66 per cent
Eosinophiles	1 per cent
Mast cells	1 per cent
Hemaglobin	75 per cent

On August 8 the lamb was very badly affected with trembles as a result of feeding expressed juice. The second blood study was made on this day. The results are as follows:

Numerical count:

Erythrocytes	16,800,000
Leucocytes	7,000

Differential count:

Neutrophiles	58 per cent
Lymphocytes, large	6 per cent
Lymphocytes, small	34 per cent
Mast cells	2 per cent
Eosinophiles	None
Hemaglobin	75 per cent

The hemaglobin remains normal and the eosinophiles disappear. There is an increase of the neutrophiles at the expense of the lymphocytes. There is a total decrease of the leucocytes and an apparent increase of the erythrocytes.

Urine Study. It was not possible to secure urine for examination before death. At autopsy a small quantity was collected through the natural passage by gentle pressure on the bladder. By the observance of this precaution, albumin from the peritoneal cavity cannot get into the urine. The result of the analysis is as follows:

Physical examination:
- Transparency—Cloudy.
- Specific gravity—1012.

Chemical examination:
- Reaction—Alkaline.
- Sugar—None.
- Albumin—Trace.
- Phosphates—Present.
- Chlorides—Present.
- Sulphates—Present.
- Carbonates—Present.

The excretion of chlorides, sulphates, and phosphates was normal and the presence of albumin alone can be regarded as an abnormality.

Protocol. The carcass presents the appearance of a normal lamb, there being no palpable lymph glands nor cutaneous and subcutaneous lesions.

The Thoracic Cavity.—The lungs are pale salmon pink in color and collapse when the thorax is opened. Neither pleuritis, pneumonia, nor bronchitis are noted. There is an excessive amount of liquid in the thoracic cavity.

The Heart—The heart is pale, flabby, and small petechiations are noted at the base along the coronary arteries. A small quantity of dark coagulated blood is found in the auricles, whereas the ventricles are empty. There is no antemortem clot.

The Abdominal Cavity.—There is no abnormal quantity of liquid in the peritoneal cavity. The intestines appear normal. There are no stomach worms in the abomasum and nodular disease and peritonitis are not present.

The Spleen is normal.

The Liver.—The liver is yellowish and when examined closely, the nutmeg appearance is found to be present. The liver is so gorged with blood that it drips from the sectioned surface. The gall bladder is full.

The Bladder contains a small quantity of cloudy urine and is slightly injected.

The Kidneys.—The kidneys have a metallic appearance. Active and passive congestion are present. The sectioned surface is pale, indicating cloudy swelling.

Microscopical Examination. *The liver* shows more or less active and passive congestion, although this condition is not so intense as in many of the other cases heretofore examined. Cloudy swelling and fatty degeneration are present.

The Kidneys.—Cloudy swelling is present. The cells of the convoluted tubules are swollen, the cytoplasm granular, and the lumina in many of the tubules are entirely obliterated. Many of the cells are in a state of necrosis. Fatty degeneration is noted in certain areas, involving the cells of the convoluted tubules. Glomerulitis is present.

The Heart.—Miescher's cysts are present. These are located in the cell substance, causing the cell wall to bulge outward. The nuclei of the heart muscle cells stain faintly. Fatty degeneration is not discernible.

The Lungs are normal.

The Pancreas is normal.

The Lymph Glands are normal.

CASE 4, TABLE X, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF LAMB 244.

	Temperature.			*Pulse.*			*Respiration.*		
Date.	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*
5–11	.....	.....	104.0	....	....	82	.....	.....	78
5–12	.....	.....	103.5	....	....	72	.....	.....	66
5–13	.....	103.0	.....	....	79	....	.....	68	.....
5–14	102.8	102.6	103.4	84	84	68	78	72	70
5–15	102.6	102.7	103.2	72	84	72	70	78	120
5–16	103.0	102.9	103.0	84	84	90	96	114	156
5–17	103.0	103.0	102.9	72	84	90	132	144	168
5–18	103.5	103.3	103.3	108	96	102	168	180	186
5–19	103.5	102.3	103.5	84	90	96	178	192	216
5–20	103.9	103.1	103.5	84	90	96	192	192	204
5–21	103.3	103.1	103.5	78	90	90	168	174	174
5–22	103.6	103.3	103.6	90	90	84	150	162	210
5–23	103.8	103.5	103.6	78	84	72	114	132	144
5–24	103.6	102.8	103.2	72	72	72	156	116	132
5–25	103.4	103.0	102.9	72	84	90	108	144	144
5–26	102.9	103.2	103.0	84	84	84	54	108	132
5–27	103.4	103.1	103.3	72	90	72	120	132	138
5–28	103.4	103.4	103.1	84	87	90	114	144	108
5–29	102.8	.....	103.0	72	....	84	84	.....	90
5–30	103.0	102.8	102.8	84	78	84	78	102	150
5–31	102.6	103.0	103.0	78	78	72	78	96	84
6– 1	103.2	103.2	103.4	84	84	84	132	144	156
6– 2	103.2	103.2	103.5	78	72	84	126	150	136
6– 3	104.1	103.8	103.9	84	81	84	144	132	156
6– 4	103.0	103.4	103.6	87	84	78	84	102	126
6– 5	103.5	103.4	103.2	78	84	78	120	132	120
6– 6	103.7	103.7	104.0	81	75	81	102	144	150
6– 7	104.1	103.6	103.8	90	84	78	96	126	120
6– 8	104.0	104.0	104.2	81	81	78	126	132	120
6– 9	103.6	103.6	103.8	84	87	78	108	120	120
6–10	103.2	104.0	103.5	84	75	72	72	96	102
6–11	103.8	104.2	104.3	78	78	84	96	114	132*
6–12	104.2	105.0	104.6	75	78	78	126	144	192
6–13	104.8	104.7	104.8	69	72	72	192	180	192
6–14	105.4	105.6	105.1	75	69	66	192	198	168
6–15	105.6	105.5	105.8	72	66	60	150	168	168
6–16	106.0	106.4	106.5	66	72	78	120	102	126
6–17	106.4	107.0	.....	60	90	....	60	78	....

*Docked.

These data indicate that there was a disturbance in temperature after the onset of symptoms.

Clinical Notes. This lamb was given twice daily one-fourth pound of cracked corn and oats mixed, and one-half pound of kale. She was suckling the mother, ewe 171, who received twice daily three-fourths pound of cracked corn and oats mixed and one-fourth pound of white snakeroot. In addition to this, she received, at noon, one pound of hay and two pounds of kale.

A manifest stiffness of the limbs was apparent on June 11. On June 13, she refused grain and ate only a small amount of kale. She appeared stiff, droopy, and dull. In the afternoon, respirations were slightly jerky. On the morning of June 14, she trembled slightly and was prone to lie down at all times. When made to stand she would tremble, and the longer she was kept on her feet the more intense the trembling. In the afternoon the symptoms were more aggravated. She trembled in all parts of the body and after a paroxysm of trembling would fall down apparently exhausted. At intervals she gritted her teeth. On the 15th, while lying down, she attempted to eat kale. Trembling became more aggravated, as did the gritting of teeth, and she appeared weaker than on the previous day. She did not eat during the afternoon. On the morning of June 17 she was found prostrate on her side. Respiration was labored, eyes were set, and legs were intermittently trembling. She died about 12:30 P. M.

Blood Study. On May 18 a study was made of the blood of lamb 244 to determine the normal condition, with the following results:

Numerical count:	
Erythrocytes	13,560,000
Leucocytes	12,000
Differential count:	
Neutrophiles	20 per cent
Lymphocytes, large	7 per cent
Lymphocytes, small	71 per cent
Eosinophiles	1 per cent
Mast cells	1 per cent
Hemaglobin	75 per cent

On June 16, after the symptoms of milksickness had developed, another study was made. The results are as follows:

Numerical count:	
Erythrocytes	15,600,000
Leucocytes	10,000
Differential count:	
Neutrophiles	44 per cent
Lymphocytes, large	6 per cent
Lymphocytes, small	49 per cent
Mast cells	1 per cent
Hemaglobin	75 per cent

There was an increase of neutrophiles at the expense of the lymphocytes and an apparent increase in the erythrocytes. The lamb had refused water for at least forty-eight hours before this second study was made, which may account for the apparent increase. The eosinophiles had entirely disappeared. The hemaglobin remained the same.

Urine Study. On June 17, when the autopsy was made, the urine was forced out of the normal outlet by gentle pressure upon the bladder and was thus kept free from albuminous material. The following is the result of the analysis:

Physical examination:
Sediment—Present.
Transparency—Cloudy.
Specific gravity—Insufficient amount for test.

Chemical examination:

Phosphates—Present.	Chlorides—Present.
Reaction—Faintly acid.	Albumin—None.
Sugar—None.	Carbonates—Present.
	Sulphates—Present.

The urine of suckling lambs is normally acid in reaction. The cloudy condition is noted in other cases of milksickness. The lamb was apparently normally eliminating the phosphates, chlorides, and sulphates.

Protocol. There are no subcutaneous nor cutaneous lesions to be found. There are no palpable lymph glands, and the external appearance is that of a normal lamb.

Thoracic Cavity.—The lungs do not collapse when the thorax is opened. There is present a congestive condition, but neither pneumonia, bronchopneumonia, nor pleuritis. The lungs are dark pink in color.

The Heart.—Petechiation at the the base of the heart along the course of the coronary arteries is noted. The right side of the heart is empty, while the left contains dark coagulated blood. There are no petechiations on the endocardium or pericardium.

The Abdominal Cavity.—There is no abnormal quantity of fluid in the abdominal cavity. There is no peritonitis. The small and large intestines are affected with nodular disease and stomach worms are present in small numbers in the abomasum. The small intestine appears injected, which condition does not exist in the large intestine.

The Spleen.—Normal.

The Kidneys.—The kidneys appear swollen and of a metallic appearance. The capsule strips off easily. Both active and passive congestion and cloudy swelling are present. Both kidneys weigh one-eighth pound.

The Musculature.—The musculature appears normal.

The Liver.—The liver is filled with blood which drips from the sectioned surface. It is nutmeg in appearance. There is evidence both of congestion and of cloudy swelling. The liver weighs one-fourth pound.

The Lymph Glands.—The lymph glands appear normal.

The Brain.—The brain appears somewhat congested.

Microscopical Examination. *The Liver.*—After hardening in formalin, sectioning, staining with hematoxylon and eosin, and clarifying in beechwood creosote, study was made of the cellular changes.

The liver shows both active and passive congestion and cloudy swelling.

The Kidneys.—Active and passive congestion are present. There is an occasional area infiltrated with polymorphonuclear leucocytes and with a few round cells. Cloudy swelling in various stages is present, thus indicating an acute parenchymatous nephritis.

The Heart.—The blood vessels are congested. There is present no fatty degeneration.

The Brain.—The cerebrum and cerebellum are both congested. The brain cells appear normal with no invasion by leucocytes.

The Lungs.—The lung tissue shows congestion, certain alveoli are filled with serum and an occasional one with a few erythrocytes.

The Pancreas—Normal.

The Spleen.—Normal.

The Adrenal Glands.—Normal.

CASE 5, TABLE XI, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF EWE 12.

	Temperature.			*Pulse.*			*Respiration.*		
Date.	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*
5–11	.....	.....	103.3	....	....	68	.....	.....	72
5–12	.....	.....	104.0	....	....	65	.....	.....	60
5–13	.....	101.4	.....	....	56	....	.....	48	.....
5–14	101.0	101.2	102.2	58	66	48	52	45	30
5–15	100.5	101.2	101.9	60	54	66	42	42	42
5–16	101.3	102.0	102.1	56	70	66	48	48	54
5–17	101.5	102.0	103.0	66	66	66	36	42	54
5–18	101.4	101.8	102.6	72	76	72	48	54	72
5–19	101.8	101.9	102.7	60	63	72	48	48	78
5–20	102.0	102.0	101.9	66	72	72	42	45	45
5–21	101.9	102.2	103.2	69	66	72	39	48	90
5–22	102.0	101.9	102.9	72	60	69	36	42	72
5–23	101.8	101.6	102.4	57	66	60	33	48	42
5–24	101.5	101.6	102.2	66	60	63	30	36	36
5–25	101.6	101.4	102.3	54	63	66	30	36	36
5–26	102.0	102.2	103.0	63	66	69	30	27	35
5–27	102.0	102.3	103.2	72	72	75	30	42	84
5–28	102.3	102.2	103.4	72	63	72	30	48	48
5–29	101.8	.....	102.6	66	....	66	42	.....	36
5–30	101.5	101.5	102.3	69	60	69	42	38	42
5–31	101.2	101.6	102.4	69	72	60	39	48	36
6– 1	101.7	102.6	103.6	69	66	78	36	54	84
6– 2	103.0	102.5	103.0	66	72	78	33	48	66
6– 3	103.1	102.8	102.8	66	66	69	54	51	60
6– 4	102.2	102.4	102.6	60	66	66	36	36	30
6– 5	102.3	102.5	103.8	66	66	72	36	23	48
6– 6	102.0	102.0	103.3	72	66	66	42	39	84
6– 7	102.3	102.6	103.8	60	66	63	36	42	54
6– 8	102.2	102.6	103.4	69	66	66	36	42	30
6– 9	101.8	102.2	102.0	60	66	69	30	36	36
6–10	102.0	102.0	102.7	66	66	60	27	30	27
6–11	101.5	101.8	103.7	72	69	66	30	27	48
6–12	101.6	102.6	103.5	69	60	66	36	48	72
6–13	102.2	103.0	103.4	63	72	68	36	66	54
6–14	102.4	102.0	103.1	72	72	66	30	75	30
6–15	102.2	102.8	103.4	72	69	72	42	36	48
6–16	102.7	102.4	103.0	69	69	72	30	30	42
6–17	102.2	102.2	103.0	72	66	63	42	66	42
6–18	102.0	102.0	104.0	66	72	66	42	36	48
6–19	102.6	102.6	102.8	69	75	66	39	84	60
6–20	102.7	102.7	103.0	66	66	69	45	60	57
6–21	102.2	103.2	103.4	66	72	66	54	60	72
6–22	102.7	102.5	102.7	72	66	66	39	48	54
6–23	102.8	103.3	103.4	66	72	69	63	78	72
6–24	102.0	102.4	103.8	72	66	78	54	72	120
6–25	102.8	103.0	103.2	63	66	66	42	72	72
6–26	102.6	102.5	103.7	60	72	72	42	60	102
6–27	102.8	102.6	103.2	72	69	69	48	72	84
6–28	102.6	102.6	103.6	66	60	69	42	54	78
6–29	102.7	102.6	102.8	69	69	72	48	54	36
6–30	102.4	102.0	103.2	69	63	69	36	54	72
7– 1	103.0	102.7	102.4	66	66	69	48	54	72
7– 2	102.6	102.5	103.0	75	72	66	36	60	48
7– 3	102.5	102.6	103.3	72	69	66	42	54	72
7– 4	101.6	102.4	102.5	72	72	69	42	63	74
7– 5	102.1	103.0	103.3	66	72	69	36	60	54
7– 6	102.6	102.8	103.0	72	69	63	42	66	54
7– 7	102.6	102.6	102.8	60	69	66	48	54	42
7– 8	102.3	103.0	102.3	66	72	69	54	60	72
7– 9	102.6	103.0	103.3	72	66	72	54	60	96
7–10	102.8	102.9	103.4	72	69	69	54	66	72
7–11	102.6	103.2	103.7	72	66	72	48	78	66
7–12	103.4	103.3	103.4	63	69	66	48	66	90
7–13	102.3	102.9	103.4	66	66	72	54	54	66
7–14	103.0	103.1	103.5	72	66	69	42	66	78
7–15	103.0	103.0	103.2	72	66	63	36	69	66
7–16	102.7	102.6	103.2	66	66	66	48	60	108
7–17	102.6	103.0	103.2	72	72	69	36	90	72
7–18	101.5	102.5	102.7	66	60	60	48	42	54
7–19	101.5	102.2	103.5	69	66	84	72	78	60
7–20	101.3	101.7	102.7	69	78	78	66	54	69
7–21	101.1	101.9	101.9	78	72	75	90	84	84
7–22	102.0	102.1	102.4	72	81	78	60	72	63
7–23	102.5	102.3	102.3	72	69	66	60	60	54

These data do not show any variation from the normal in temperature, pulse, or respiration.

Clinical Notes. On July 17 ewe 12 appeared droopy, dull, and stood with eyes half-closed. On the 19th breathing was jerky and trembling was noted in both fore and hind limbs. After she had lain quiet for a while she would stand for several minutes, and with the onset of trembling would lie down again. Her appetite was good. On July 21 the symptoms were more aggravated. She would stand with all four feet close together under the body, with back arched, and was quite stiff. On the 22d, trembling was more violent, but her appetite remained good. In the afternoon, she passed into a comatose condition. There was little appreciable change on July 23, but the symptoms were more aggravated. On July 24 she was killed and an autopsy was performed.

It should be noted with reference to this ewe that she had recovered from trembles from feeding experiments of the previous year. This indicates that one attack does not render immunity to a subsequent attack, a fact in keeping with popular belief.

Blood Study. On May 18 a study was made of the blood of ewe 12 to determine its normal condition. The following is the result:

Numerical count:	
Erythrocytes	8,240,000
Leucocytes	12,000
Differential count:	
Neutrophiles	47 per cent
Lymphocytes, large	7 per cent
Lymphocytes, small	40 per cent
Eosinophiles	3 per cent
Mast cells	None
Hemaglobin	70 per cent

On July 22, after symptoms of trembles had become well developed, another blood study was made with the following result:

Numerical count:	
Erythrocytes	8,320,000
Leucocytes	5,000
Differential count:	
Neutrophiles	66 per cent
Lymphocytes, large	8 per cent
Lymphocytes, small	22 per cent
Eosinophiles	None
Mast cells	4 per cent
Hemaglobin	75 per cent

There was an increase of neutrophiles at the expense of the small lymphocytes. There was a disappearance of the eosinophiles and the appearance of mast cells. The hemaglobin remained practically the same and there was no change in the number of erythrocytes. There was a considerable decrease in the leucocytes.

Urine Study. An analysis of the urine was made on June 18, with the following results:

Physical examination:

Transparency—Pale straw color.

Specific gravity—1014.

Chemical examination:
Reaction—Alkaline.
Sugar—Present.
Albumin—Present.
Phosphates—Present.
Carbonates—Present.
Chlorides—Present.
Sulphates—Present.

On July 19, after the symptoms of trembles were well developed, the urine was again analyzed. The following is the result of this analysis:

Physical examination:
Transparency—Brownish yellow.
Sediment—Present.
Specific gravity—1030.

Chemical examination:
Reaction—Neutral.
Sugar—Present.
Albumin—Present.
Carbonates—Present.
Sulphates—Present.
Chlorides—Present.
Phosphates—Present.

Microscopic examination:
Tube casts—Present.
Character of casts—Granular (Fig. O).
Epithelial cells—Round, squamous, elliptical.

Protocol. Externally the body presents nothing on inspection that is to be considered worthy of note. There are no subcutaneous lesions of any kind to be found.

Thoracic Cavity.—There is no pleuritis. The lungs do not collapse when the thorax is opened. The color of the lungs is a purplish-salmon. No edema, pneumonia, nor broncho-pneumonia are present. No ecchymoses are found on the pleural surface.

The Heart.—There is slightly more fluid than is normal in the pericardial sac. Small petechial areas occur over the base of the heart. There is no pericarditis nor endocarditis. The right side of the heart is empty and the left side contains dark, coagulated blood, post mortem coagulation. The heart muscles appear pale.

The Abdominal Cavity.—There is no abnormal quantity of fluid in the abdominal cavity. The small and large intestines are affected with nodular disease. Few stomach worms are to be found in the abomasum. The small intestine is highly injected and the large intestines appear normal in this respect.

The Spleen.—Normal.

The Kidneys.—The kidneys appear swollen, the capsule having a metallic appearance. Both active and passive congestion are discernible. Cloudy swelling is present. Both kidneys weigh four and one-half ounces.

The Liver.—The liver shows the characteristic discoloration and blood flows freely from the sectioned surface.

The bladder.—The bladder is injected and contains a small quantity of urine.

Musculature.—The musculature is normal in appearance.

The Brain.—The brain, as well as the coverings, appear congested.

The Lymph Glands.—All visceral and body lymph glands appear normal.

Microscopical Examination. *The Liver.*—The tissues were first hardened in formaldehyde, sections were then made, which were stained in hematoxylon and eosin, and clarified in beechwood creosote.

The liver shows both active and passive congestion, cloudy swelling and fatty degeneration.

The Kidneys.—The kidneys show both active and passive congestion. Cloudy swelling and glomerulitis are present. Some of the cells of the convoluted tubules have lost their nuclei and are in a state of necrosis. In some areas the lumina are not discernible and the bases of the cells have separated, the whole mass pushing toward the center. Some of the tubules show evidence of fatty degeneration.

The Brain.—The blood vessels are congested. An occasional polymorphonuclear leucocyte and quite a number of plasma cells are in each microscopic field. The brain cells appear normal and are not shrunken.

The Heart.—The heart muscle fibers have lost their cross-striation. Many parts show fatty degeneration. The nuclei stain deeply, in fact, are picnotic. The blood vessels are congested.

The Lungs.—The lungs are hyperemic. Some alveoli are filled with serum. There is no bronchitis nor pneumonia.

The Duodenum.—Much round-celled infiltration and hyperemia are evident.

The Pancreas.—Normal.

The Adrenal Gland.—Normal.

CASE 6, TABLE XII, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF LAMB 237.

	Temperature.			*Pulse.*			*Respiration.*		
Date.	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*
5–11	.....	.....	104.6	....	....	70	.....	.....	72
5–12	.....	.....	103.6	....	....	72	.....	.....	72
5–13	.....	103.8	.....	....	76	....	.....	84	.....
5–14	102.7	101.8	103.0	78	78	48	60	72	60
5–15	104.2	104.1	103.5	84	90	72	84	108	108
5–16	102.1	102.7	103.1	84	72	78	72	78	96
5–17	102.3	102.3	103.0	78	80	84	90	102	144
5–18	102.6	103.0	102.7	78	80	78	144	156	150
5–19	102.9	102.6	102.9	80	84	78	178	190	198
5–20	102.5	102.1	102.5	90	90	84	180	186	182
5–21	103.1	103.2	103.4	78	78	84	193	163	144
5–22	102.6	102.8	103.5	78	90	84	138	162	156
5–23	103.2	103.0	103.0	90	84	78	126	144	120
5–24	102.8	102.6	103.2	78	84	78	84	102	96
5–25	103.0	103.2	103.0	72	75	78	108	108	108
5–26	103.0	102.8	103.2	84	75	84	90	102	102
5–27	103.4	103.0	103.2	75	75	78	84	114	108
5–28	103.4	102.9	103.0	72	66	72	102	78	72
5–29	103.0	.....	102.9	72	....	84	66	.....	60
5–30	103.2	103.0	103.1	72	69	75	60	108	120
5–31	102.6	102.5	102.8	78	84	78	72	78	102
6– 1	103.4	103.1	103.8	84	78	78	120	147	144
6– 2	102.8	103.0	103.0	72	84	72	126	132	132
6– 3	103.5	103.7	103.6	81	78	84	156	138	120
6– 4	102.8	103.0	103.2	72	84	72	66	69	96
6– 5	103.2	103.0	103.2	81	72	75	102	120	114
6– 6	103.4	103.2	103.6	72	81	75	102	108	108
6– 7	103.6	103.0	104.2	72	78	84	108	96	120
6– 8	103.4	103.2	103.6	75	72	72	108	120	108
6– 9	103.0	103.6	103.5	72	72	75	84	108	84

	Temperature.			Pulse.			Respiration.		
Date.	A.M.	M.	P.M.	A.M.	M.	P.M.	A.M.	M.	P.M.
6–10	103.4	103.8	103.7	72	72	75	48	75	54
6–11	103.2	103.0	104.5	78	78	81	48	84	108
6–12	103.8	103.5	103.8	84	75	72	126	120	132
6–13	104.1	104.0	104.2	75	78	72	120	126	144
6–14	104.0	104.0	103.3	78	75	75	108	120	90
6–15	103.6	103.5	104.0	78	78	78	66	60	84
6–16	103.0	103.8	104.0	78	78	72	60	54	60
6–17	103.4	103.3	104.1	78	72	72	66	78	72
6–18	102.8	103.4	104.1	75	75	72	78	102	96
6–19	103.6	103.7	104.0	78	78	75	84	90	114
6–20	103.4	103.9	104.2	72	72	72	90	84	96
6–21	104.0	104.1	104.4	78	75	72	84	96	102
6–22	103.7	103.5	103.8	72	72	75	78	108	96
6–23	104.4	103.3	104.4	78	75	78	84	108	104
6–24	104.0	104.2	104.6	78	75	75	90	120	144
6–25	104.1	104.2	104.4	66	75	72	126	126	144
6–26	103.6	103.9	104.6	69	72	81	78	120	120
6–27	104.6	104.5	105.0	78	72	72	120	138	126
6–28	104.6	104.4	104.0	78	78	72	90	108	114
6–29	104.0	104.1	104.0	75	72	72	90	102	66
6–30	103.8	103.4	104.0	72	72	78	72	96	102
7– 1	103.7	104.0	104.2	69	69	72	78	108	78
7– 2	104.2	103.8	103.0	72	75	72	90	99	78
7– 3	103.2	103.7	103.4	69	66	54	60	66	66
7– 4	103.0	103.6	103.8	72	69	60	66	90	90
7– 5	103.9	103.5	103.8	81	72	66	90	96	120
7– 6	104.2	103.6	103.4	72	66	72	78	60	84
7– 7	103.6	103.6	103.7	69	66	72	66	42	72
7– 8	103.9	103.3	103.6	60	69	60	48	84	72
7– 9	104.0	103.6	104.2	66	69	66	90	96	90
7–10	103.3	103.8	104.7	66	63	72	60	102	120
7–11	103.8	103.8	104.0	69	66	78	72	54	66
7–12	103.8	103.7	104.1	60	66	69	72	96	78
7–13	103.8	103.5	103.8	72	66	69	51	72	84
7–14	103.8	103.5	103.8	66	66	72	48	102	114
7–15	104.1	103.9	104.2	66	66	72	60	90	96
7–16	104.1	103.9	104.2	63	60	66	54	60	96
7–17	104.0	104.0	103.8	66	69	66	96	96	72
7–18	103.5	103.4	103.6	60	63	66	54	60	66
7–19	103.2	103.8	104.2	63	66	57	48	54	48
7–20	103.0	103.7	103.1	66	66	60	72	57	42
7–21	102.7	103.0	103.8	57	60	63	48	51	54
7–22	104.1	104.3	103.7	69	66	66	60	84	84
7–23	104.0	104.1	104.5	60	60	60	66	84	96
7–24	104.0	104.4	104.1	66	69	66	78	114	84

Clinical Notes. On July 30 at 2:30 P. M. lamb 237 was taken from the pasture, placed in the experimental pen and given 500 c.c. of expressed juice. He refused his feed in the evening. Next morning breathing was short and labored and he gritted his teeth. He ate about one-fourth pound of oats and was given 500 c.c. more of juice. At 3 P. M. a third quantity of 500 c.c. was given. He refused his feed in the evening. On the morning of August 1 he was found dead.

Protocol. The external appearance of the carcass is that of a normal lamb.

The Thoracic Cavity.—Neither pleuritis nor pneumonia is present. The lungs are a pale salmon color and collapse when the thoracic cavity is opened.

The Heart.—There is no excessive fluid in the pericardial sac. A small amount of coagulated dark blood is found in the left side, the right being empty. The heart muscle appears normal.

The Abdominal Cavity.—The abdominal cavity does not contain an excessive amount of fluid and there is no peritonitis present. The bladder is empty and appears normal. The stomach and small and large intestines appear normal. Neither nodular disease nor stomach worms are present.

The Spleen.—Normal.

The Musculature.—Normal.

The Brain.—Normal.

The Lymph Glands—Normal.

The Liver.—The liver appears normal in color and size. The gall bladder is full.

The Kidneys.—The capsule has a metallic appearance and can easily be stripped off. Both active and passive congestion are evidenced. The grayish appearance of the parenchyma also gives evidence of cloudy swelling.

Microscopical Examination. *The Liver.*—Active and passive congestion and cloudy swelling are present.

The Kidneys.—Glomerulitis and cloudy swelling are present. In some areas the nuclei take little or no stain and in others the cells have lost their nuclei. The lumina in these areas are occluded and many cells are thus in a state of necrosis. Some cells are in a state of picnosis. Certain of the tubules show fatty degeneration.

The Pancreas.—Normal.

The Adrenal Glands.—Normal.

The Lungs.—Normal.

The Heart.—Normal.

CASE 7, TABLE XIII, SHOWING TEMPERATURE, PULSE, AND RESPIRATION OF LAMB 242.

	Temperature.			*Pulse.*			*Respiration.*		
Date.	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*	*A.M.*	*M.*	*P.M.*
5–11	.....	.....	104.6	....	....	67	.....	.....	42
5–12	.....	.....	104.0	....	....	66	.....	.....	72
5–13	.....	103.0	.....	....	84	....	.....	72	.....
5–14	102.8	102.4	102.7	76	80	66	72	78	42
5–15	102.6	102.9	103.1	63	78	78	60	66	96
5–16	102.3	102.6	103.1	60	72	96	48	63	90
5–17	103.1	102.6	102.6	78	96	86	78	114	120
5–18	103.1	103.0	103.0	96	96	96	138	172	180
5–19	103.6	103.6	103.1	78	84	90	150	160	192
5–20	103.0	102.7	102.8	78	90	90	144	150	163
5–21	103.4	102.8	103.3	84	84	96	168	144	168
5–22	103.6	102.8	103.4	84	84	72	156	150	162
5–23	103.4	103.2	103.5	78	90	84	120	138	144
5–24	103.0	102.8	103.0	78	72	84	114	102	108
5–25	103.0	103.0	103.2	78	71	87	120	138	132
5–26	103.0	103.8	103.8	78	90	90	90	120	150
5–27	103.0	102.4	103.2	84	90	87	123	152	150
5–28	103.2	103.2	103.1	90	75	84	138	126	108
5–29	103.0	.....	102.9	84	....	84	96	.....	90
5–30	102.7	102.6	103.3	90	84	84	96	102	108
5–31	102.8	103.0	103.0	90	78	78	72	96	114
6– 1	103.3	103.4	103.4	69	78	90	102	144	150
6– 2	103.1	103.0	103.9	81	78	90	126	132	114
6– 3	103.3	103.0	103.9	81	90	87	138	120	168
6– 4	102.7	103.0	103.7	78	84	84	84	96	102
6– 5	103.2	102.9	102.8	78	78	75	78	132	102
6– 6	103.5	103.7	104.0	87	72	87	132	150	162
6– 7	103.9	103.6	104.2	84	78	81	126	120	144
6– 8	104.2	103.8	103.8	81	87	90	132	138	124
6– 9	103.6	103.2	103.9	84	78	84	108	120	132
6–10	103.4	103.6	103.5	81	84	72	72	96	78
6–11	103.3	103.5	104.2	81	84	78	90	126	138*
6–12	104.2	104.2	105.1	78	78	72	150	156	144
6–13	104.1	104.7	105.3	78	84	84	132	150	162
6–14	105.8	105.6	105.4	72	72	84	192	180	132
6–15	105.0	105.0	105.1	69	72	66	60	114	138
6–16	105.9	106.2	Died	66	66	....	108	60	.....

*Docked.

Clinical Notes. On the morning of June 13 there was a manifest stiffness of the legs. The next day the lamb stood with head down and back bowed. On the 15th she did not touch the kale or grain and upon being exercised

began to tremble. She did not remain long on her feet, but lay down as though exhausted. Trembling was aggravated with the additional symptoms of vomiting, frothing at the mouth, grating of the teeth, and labored breathing on the 16th. She died at 1:30 P. M.

Blood Study. On May 18 a study was made of the blood to determine the normal condition of this lamb's blood with the following result:

Numerical count:	
Erythrocytes	13,040,000
Leucocytes	14,000
Differential count:	
Neutrophiles	20 per cent
Lymphocytes, large	16 per cent
Lymphocytes, small	61 per cent
Eosinophiles	3 per cent

On June 15, after the symptoms had developed, another study of the blood was made with the following results:

Numerical count:	
Erythrocytes	14,000,000
Leucocytes	11,000
Differential count:	
Neutrophiles	46 per cent
Lymphocytes, large	2 per cent
Lymphocytes, small	52 per cent
Eosinophiles	None

This shows an increase of neutrophiles with a corresponding decrease of lymphocytes. The eosinophiles have disappeared. There is a decrease in the total number of leucocytes, and apparently a slight increase of erythrocytes.

Protocol. There are no cutaneous or subcutaneous lesions to be found. The lymph glands are not palpable and the external appearance is that of a normal lamb.

The Thoracic Cavity.—The lungs are of pale salmon color and collapse when the thorax is opened. There is present neither pneumonia nor pleuritis.

The Heart.—The heart weighs one-fourth pound. It shows small petechiæ along the course of the coronary arteries. The heart muscle appears normal.

The Abdominal Cavity.—The quantity of fluid in the abdominal cavity is normal and there is no peritonitis. The small and large intestines appear normal.

The Spleen.—Normal.

The Musculature.—Normal.

The Kidneys.—The kidneys are very dark in color and the surface appears slightly mottled, due to intense congestion. Both active and passive congestion are present. The sectioned surface is grayish, indicating cloudy swelling. Both kidneys weigh one-eighth pound. The capsule strips off easily.

The Adrenal Glands.—Normal.

The Lymph Glands.—Normal.

The Liver.—The liver is normal in color. It weighs one and one-eighth pounds. The gall bladder is full.

The Brain.—The coverings and brain substance are normal in appearance.

Microscopical Examination. *The Liver.*—Fatty degeneration, active and passive congestion and cloudy swelling are present.

The Kidneys.—Active and passive congestion are present. The nuclei of the parenchymatous cells, in some areas, are picnotic; in others, they stain faintly. The protoplasm is granular and the cells swollen. The lumina of certain tubules are partially occluded and in some places the lumina of the convoluted tubules have disappeared. The nuclei, especially of these convoluted tubules, have entirely disappeared and the cells are in a state of necrosis. Many of the glomerules appear shrunken and a wide space can be noted between the capillary plexus and the capsule of Bowman. Thus acute parenchymatous nephritis with glomerulitis and active and passive congestion are present.

The Heart.—The blood vessels are congested.

The Brain.—The brain is congested. This congestion involves both arteries and veins. The spinal cord also shows congestion.

The Lungs.—Normal.

The Pancreas.—Normal.

The Adrenal Gland.—Normal.

The following microscopic studies were made of the livers and kidneys of six guinea pigs:

Microscopical Examination. CASE 1.—Acid extract, No. 1.

Liver.—Congestion, fatty degeneration, and cloudy swelling are marked. Congestion, both active and passive, is more intense than in sheep.

Kidneys.—The changes in the kidneys include active and passive congestion, fatty degeneration, and cloudy swelling.

CASE 2.—Green stems, No. 2.

Liver.—Cloudy swelling, fatty degeneration, and active and passive congestion are all present. An occasional area is invaded by polymorphonuclear leucocytes.

Kidneys.—The metamorphoses include active and passive congestion, cloudy swelling, and glomerulitis.

CASE 3.—Green leaves.

Kidneys.—Glomerulitis, active and passive congestion, and cloudy swelling are very pronounced.

Liver.—Active and passive congestion and cloudy swelling are present. There are fatty degenerative changes in some areas.

CASE 4.—Expressed juice, No. 1.

Liver.—Active and passive congestion and cloudy swelling are apparent. There are, furthermore, areas showing the beginnings of fatty degeneration.

Kidney.—The pathological changes include active and passive congestion, cloudy swelling, and glomerulitis.

Cultural studies were made of the blood from the liver, kidneys, and heart. Three tubes of agar were inoculated and all except one were negative. In this tube, a polar staining, short bacterium was isolated in pure culture. Intraperitoneal inoculation on guinea pigs resulted in no evidence of disease. The germ in question was, therefore, considered as a contamination.

Case 5.—Expressed juice, No. 2.

Liver.—Cloudy swelling and fatty degeneration are present. This liver does not show active or passive congestion.

Kidneys.—Active and passive congestion are present. Cloudy swelling is well advanced in the convoluted tubules, in many of which the cells are in a state of disintegration.

Case 6.—Green leaves, No. 2.

Liver.—Fatty degeneration was more advanced than in Case 4. Active and passive congestion are present.

Kidneys.—Active and passive congestion and cloudy swelling are seen in the renal tissues. Some of the convoluted tubules show fatty degeneration.

The following report covers the clinical examination of one hog which died during the feeding experiments:

Urine Study. An analysis of the urine shows the reaction to be acid. The specific gravity is 1014. Tests for albumin and sugar were negative.

Protocol. There are no subcutaneous or cutaneous lesions to be found, and no palpable lymph glands. The external appearance presents the picture of a young hog in a poor condition of flesh. The conjunctiva are pale.

Thoracic Cavity.—The lungs do not collapse when the thorax is opened, and certain of the lobules show congestion. When the sectioned surface of the lungs is examined, the bronchi are found to contain a frothy material.

The Heart.—The heart muscle appears pale, but there is no petechiation. There is present a slight evidence of a hydropericardial condition, and the pleura is normal.

The Abdominal Cavity.—The peritoneum, spleen and lymph glands are normal. The liver presents a pale, parboiled appearance, the lobules show very distinctly, and from the sectioned surface can be scraped a material which has the appearance of fat, and ignites when held in a flame. Duodenitis is present.

The Kidneys.—The kidneys appear normal in size and are of the same parboiled appearance as was noted in the case of the liver.

The Bladder.—Filled with urine.

The Musculature.—The general musculature of the body appears paler than normal.

Microscopical Examination. *The Liver.*—The liver shows both cloudy swelling and fatty degeneration in rather advanced stages.

The Kidneys.—Fatty degeneration is evident as are also various stages of cloudy swelling.

The Heart.—The nuclei stain pale, but the muscle cells have not lost their cross-striation.

The Brain.—The brain, both cerebrum and cerebellum, appear normal.

The Lungs.—Some lobules show edema and congestion.

The Pancreas.—Normal.

The Spleen.—Normal.

The Adrenal Glands.—Normal.

Cultural Examination. No growth appeared in attempted isolations of organisms from the blood of the kidney and liver of this animal.

SUMMARY OF LESIONS

The following is a tabulation of the lesions of sheep and lambs dead of trembles and milksickness, from a total of 16 cases:

Gross	*No.*	*Per cent*
Petechia, epicardium	13	81
Pale heart muscle	3	18
Muco-enteritis, small intestine	12	75
Active and passive congestion, kidneys	15	93
Cloudy swelling, kidneys	15	93
Congestion of brain and meninges	6	37
Lungs do not collapse, slight edema	5	31
Congestion, liver	12	75
Cloudy swelling, liver	12	75
Hydropericardium*	4	25

The following is a tabulation of the microscopic study of the organs of 16 sheep and lambs dead of trembles:

Microscopic		
Liver:	*No.*	*Per cent*
Active congestion	9	56
Passive congestion	8	50
Cloudy swelling	13	81
Fatty degeneration	14	87
Kidneys:		
Active congestion	8	50
Passive congestion	7	43
Cloudy swelling	16	100
Glomerulitis	9	56
Fatty degeneration	5	31
Brain:		
Congestion†	8	50
Heart:		
Fatty degeneration	5	31
Congestion	4	25
Lungs:		
Hyperemia	5	31
Edema	4	25
Duodenum:		
Muco-enteritis	12	75

The most striking pathological features in trembles or milksickness are therefore the albuminoid and fatty metamorphoses of the parenchymatous organs.

*These sheep were infested with Hemonchus contortus, which may account for any hydropericardium present.

†Only twelve cases were studied microscopically.

Cultures were made from livers, hearts, and kidneys of a total of six sheep and lambs and one hog dead of the disease, all of which cultures were negative. Cultures were made from the heart, liver and kidneys of a guinea pig dead of the disease, one of which cultures showed a growth, which organism later proved to be a contamination.

NATURE OF THE POISONOUS PRINCIPLE

Since a relatively recent claim has been made (Moseley, 1909) that the feeding of aluminium phosphate is followed by effects similar to those following the feeding of white snakeroot, an attempt was made in 1916 to produce trembles by feeding aluminium phosphate to sheep. Two ewes, 166 and 167, were accordingly maintained on this experiment from September 9 to November 17. During this time each ewe was fed 412 gm. of aluminium phosphate ($Al\ PO_4$; Baker's C. P.) mixed with 68.5 pounds of grain, this being supplemented with 138 pounds of alfalfa hay. The daily amounts of aluminium phosphate given were gradually increased from 2 to 16 gm.

At no time during this period of 69 days were these ewes observed to manifest any symptoms of trembles. The initial weight of ewe 166 was 80 pounds, and her weight at the close of the experiment was 91 pounds. The initial and final weights of ewe 167 were 90 and 93 pounds, respectively.

These results indicate that aluminium phosphate is not the active principle in white snakeroot and are in accord with statements more recently made by Moseley (1917).

Certain of the experiments with sheep and guinea pigs which were made in 1917 indicate a number of points with reference to the nature of the active substance in the production of trembles and milksickness. No evidence has been obtained that it is water soluble, or alcohol soluble, and evidence of its solubility in dilute acid is inconclusive. With long desiccation at a temperature of about 100 degrees C., the substance seems to lose its toxicity. Such is not the case when the expressed juice is evaporated at about 60 degrees C. The plant furthermore contains a nontoxic volatile oil which does not pass into the milk; at least it has not been possible in the several attempts which have been made to distil it from milk from a cow fed on white snakeroot. There is furthermore present a considerable amount of resinous material which, according to a recent account by Moseley (1917), exists in the leaves to the extent of 9 per cent of their dry weight and is the poisonous principle. This claim, however, is not supported by conclusive experimental data.

A number of the more common reagents for alkaloids were employed on the presumption that the plant contains an alkaloid, which is the active principle. No precipitate appeared when Mayer's reagent was added to expressed sap. Potassium ter-iodide, phosphotungstic acid, auric chlorid and platinic chlorid failed to yield precipitates. With a saturated solution of tannic acid, however, a copious precipitate appeared. Since many organic substances are precipitated with tannic acid, and since negative results were secured with all of the other common precipitants, there is little likelihood of the presence of an active alkaloid in white snakeroot.

Since the glucosides, eupatorin and euparin, are known to occur in Eupatorium perfoliatum and E. purpureum respectively, two species commonly present within the State, and since certain glucosides are known to possess toxicological properties, Bourqelot's general group test for the presence of reducing sugars after hydrolysis was made. A quantity of the expressed sap of the plant was made acid by the addition of 1 per cent by volume of concentrated hydrochloric acid and permitted to stand for twenty hours before analysis. Another portion was kept for an equal period of time at about 30 degrees C. to favor activity by enzymes within the sap. A third quantity was freshly expressed when needed for analysis. One hundred cubic centimeters of each sample were diluted with 400 c.c. of water, clarified with alumina cream and an aliquot, then taken for analysis. The official method* for the estimation of reducing sugars was followed. The results of this analysis showed the presence of approximately .10 gm. of reducing sugar in 100 c.c. of freshly prepared sap, of .13 gm. in 100 c.c. when enzymes within the expressed sap were permitted to act, and of .20 gm. in 100 c.c. when dilute acid was used. Hydrolysis, therefore, resulted from enzymotic activity and from the use of weak acid. This may be taken to indicate the presence of glucosides in the sap of white snakeroot. It is realized, of course, that there may occur within plants substances which can reduce Fehling's solution without themselves undergoing preliminary hydrolysis, and that substances other than glucosides yield glucose on hydrolysis. Further studies on the nature of the active principle are in progress.

No particular difficulty need be encountered in explaining the excretion of this poisonous principle in the milk, a fact which has long been supported by more or less experimental evidence prior to the present studies. It is a matter of common knowledge that milk acquires tastes and flavors from the feed of the animal. This in itself is proof

*Wiley, H. W., ed. Official and provisional methods of analysis, Association of Official Agricultural Chemists. As compiled by the committee on revision of methods. U. S. Dept. Agr. Bur. Chem. Bul. 107 (rev.), p. 42, 1912.

that foreign substances find entrance into the milk. Furthermore, the medical practitioner well knows that such substances as opium, morphine, and atropin may pass into the mother's milk and act on the nursing child. Not only do organic substances pass into the milk, but many inorganic substances as well,‡ as arsenic, iodine, lead, zinc, mercury, iron, bismuth, and antimony.

Means of Prevention and Cure

Prophylactic or preventive measures, rather than curative measures, are to be employed in dealing with trembles and milksickness, particularly in the case of domestic animals. In districts where the disease was prevalent, early settlers found, by keeping their animals from pasturing upon certain lands or by cutting down the timber and exposing the land to sunlight, that they could avoid the disease. They furthermore found that by plowing dangerous areas and seeding them to cultivated forage plants, they could render them safe for their stock. The employment of either of these preventive measures is in some localities practicable under North Carolina conditions. Where the timbered lands are under the control of timber companies it is not feasible to clear them, and furthermore it would in many places not be advisable to do so because of the value of the timber. If it is possible to clear the land, it should be done since white snakeroot is intolerant to full sunlight. Areas occupied by this weed might in some cases be fenced off, some of them might be mown several times during a growing season, or might even be plowed up. Since the weed is perennial rooted, a single mowing off of the tops, or even a single plowing, would not destroy all of the plants. The destruction of at most a few acres of white snakeroot will in many large pastures render an otherwise dangerous pasture harmless.

Various forms of treatment have been suggested for animals suffering from the disease, but the nature of the changes within the internal organs, as has been described, are such as to extend little hope that beneficial results can follow medication. Among the classes of drugs which veterinarians employ are cathartics such as eserin, internal antiseptics, and nerve stimulants, but without consistent remedial effects. Large doses of sodium bicarbonate are relied upon by others to effect a cure.

Our own experimental work on this phase of the problem has been confined to the use of common salt and baking soda, since the accounts of Moseley (1910) and others suggest that sodium compounds have anti-

‡ *Vide*, Hammarsten and Hedin, a text-book of Physiological Chemistry, 7th edit., 1914, p. 671.

dotal effects. Three animals were employed in this experiment, which was conducted between September 18 and October 20, 1916. The essential facts in this experiment are assembled in Table XIV.

TABLE XIV.—RESULTS OF FEEDING WHITE SNAKEROOT TOGETHER WITH SALT OR SODA TO SHEEP.

Ewe No.	*Initial weight Pounds*	*Placed on feed*	*Date of death*	*Days before death resulted*	*Weight at death Pounds*	*Feed consumed*	
						Grain Pounds	*Weed Pounds*
21	121	Sept. 18	Sept. 29	11	.....	8	5.25
28	96	Sept. 18	Oct. 7	19	73.5	15	10.25
37	118	Oct. 20	Oct. 20	18	78.5	10	6

Ewe 21 consumed 8 ounces of salt and ewe 37 ate 12 ounces during the periods of 11 and 18 days, respectively, in which they were on the experiment. Ewe 28 ate with her feed 30 ounces of baking soda. Salt and soda in these amounts given along with a ration of grain and white snakeroot are therefore without apparent antidotal effect.

The early treatments employed by physicians were drastic, since among them were blood-letting and strong purgatives. Graff (1841) advised the use of calomel, whereas Drake (1841) and Philips (1877) both advised against it. The latter used strychnine apparently with benefit. The allaying of abdominal pain by counter irritation over the stomach was a much used measure. Another favorite measure, which is at present much used, is the giving of liberal quantities of brandy and honey or brandy and milk (Dumm, 1880). Sodium bicarbonate is believed by Walsh (1909) to be efficacious. Medical treatises as recent as that of Hare (1907)* give no specific, but simply state that the treatment is purely symptomatic and consists of the judicious use of stimulants and sedatives as they may be needed.

General Summary

1. A disease of domestic animals commonly called trembles, because trembling is the most prominent symptom, has been the subject of investigation at this Station for two seasons. This disease is also called milksickness since man may contract the disease by the ingestion of milk products from cows affected with trembles. Attention in this investigation has been directed primarily to the etiology, transmission, symptomatology, and pathological anatomy of the disease.

2. A study of the literature on this disease reveals the fact that it has existed in North Carolina since the days of the American Revolution, and that the first published account appeared in 1810. The disease was, no doubt, more commonly present during the early part of the past century than is now the case.

3. Many accounts have been published dealing with the causation of trembles and milksickness. Some of these causes are more or less fanciful, while

*Hare, H. A. A text-book of the practice of medicine, 2d edit., 1907. Philadelphia and New York.

the others may be classified as supporting either (1) the mineral poison theory, (2) the germ or microbic theory, or (3) the poisonous plant theory.

4. The first claim that white snakeroot, Eupatorium urticæfolium, is responsible for the disease seems to have been made as early as 1840. The observations and experiments of several subsequent writers support this claim as do the present experimental studies.

5. There are about forty species of Eupatorium in the southern United States, none of which species except white snakeroot are known to be poisonous, although several species are used medicinally. White snakeroot is commonly present in shady, mountainous situations in western North Carolina, and is distinguishable with difficulty from some of the species of Eupatorium, except by one with experience in identifying plants and by the exercise of close observation.

6. In previous accounts, the symptoms of the disorder appear to have been described in detail only in the case of cattle and of man. The writers have not had occasion to see the disease in cattle or in man and in their studies have employed ewes, lambs, hogs, dogs, guinea pigs, and mice. Trembles was developed in sheep, hogs, and guinea pigs, and the symptoms of the disorder have accordingly been described with considerable fullness and illustrated photographically. The symptoms in sheep and hogs are sufficiently characteristic so that any one who has ever seen an affected animal may be certain of his diagnosis.

7. The disease may appear at any season of the year, but is most prevalent in late summer and autumn especially when other vegetation is scarce because of drought. The disease is frequently fatal in domestic animals while the sequel of milksickness in man, in case of recovery, is lasting debility.

8. The present experiments were conducted at West Raleigh, N. C., about 400 miles distant from the place of collection of the white snakeroot used, and no case of trembles or milksickness had ever appeared in West Raleigh prior to the performance of these feeding tests.

9. During the experimentation, 31 fatal cases of trembles and milksickness have been developed among the 44 ewes and lambs that were employed in some phase of the experimentation involving the feeding of white snakeroot. Two of these lambs contracted genuine cases of milksickness by suckling their mothers, demonstrating that the disease may be transmitted through the milk. This fact has for a long time been a matter of common belief among farmers. Furthermore, animals in lactation, having access to white snakeroot, may be apparently normal yet are capable of transmitting milksickness through their milk.

There was no other contributory cause of death of these 31 animals except in the case of two individuals, in which cases stomach worms may have been, in part, responsible for death.

One of the two hogs employed in the experiment developed a typical case of trembles.

Fifteen of the 29 guinea pigs died from the feeding of white snakeroot or its products.

It is not possible to determine with certainty whether death resulted from the feeding of butter in the case of two of the three mice employed, although it is logical, in view of the experiments with suckling lambs, to believe that the disease may be transmitted through the agency of butter.

No evidence has been secured that the flesh of sheep dead of trembles is capable of transmitting the disease to dogs, although 11 carcasses were eaten by 7 dogs.

Animals appear to differ greatly in their susceptibility to poisoning, since some became affected within a week after feeding on white snakeroot was begun, others only after several weeks, and a few remained unaffected.

10. No detailed studies of the pathological changes accompanying this disease, other than those of Jordan and Harris, have been made prior to the present study. The reports on previous studies seem all to be couched in vague, general terms. The present findings agree essentially with those of Jordan and Harris.

11. No febrile condition is present in affected sheep. The most prominent changes noted in the 22 autopsies on sheep which were performed consist of albuminoid and fatty metamorphoses of the parenchymatous organs. The lesions commonly include petechiation of the epicardium; the presence of a metallic color of the kidneys, which exhibit active and passive congestion and cloudy swelling; a "nutmeg" appearance of the liver which has undergone fatty changes, and is congested so that blood drips freely from the sectioned surface; the occurrence of muco-enteritis of the small intestine; and the presence of a congestive condition of the brain and meninges.

12. All attempts to isolate a specific organism from the internal organs of six sheep, one hog, and one guinea pig were unsuccessful. This is supported indirectly by failure of diseased animals to communicate trembles to healthy ones when they are confined together and fed from the same trough.

13. The active principle is probably glucosidal in nature.

14. The sodium compounds, salt and soda, appear not to possess antidotal effects. In view of the grave cellular changes within the internal organs, there is little hope of the efficacy of medication with domestic animals and preventive rather than curative measures are to be employed.

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EXPLANATION OF PLATES

PLATE 1.

Eupatorium urticæfolium, or white snakeroot, showing the character of the leaves and flowers.

PLATE 2.

FIG. A—Ewe 161 in a characteristic standing posture assumed when the animal is seized with a paroxysm of trembling.

FIG. B—The same animal a few minutes later when the tremors have become more acute. The animal here, as in Fig. A, has spread apart the feet in an effort to remain standing.

PLATE 3.

FIG. C—At this stage of trembling, a few seconds subsequently, the animal is beginning to drop down to a resting posture.

FIG. D—A characteristic resting posture assumed by Ewe 161 after a violent spasm of trembling. Note that the eyes are closed, the ears droop, and the chin is resting upon the ground.

PLATE 4.

FIG. E—Ewe 12 in another resting posture commonly assumed by affected animals. The same evidences of stupor are present, but the head and neck are extended.

FIG. F—A state of coma has set in and the animal (Ewe 12) is no longer able to rise.

PLATE 5.

FIG. G—Lamb 244 in a comatose condition, and her mother (Ewe 171) who is entirely normal.

FIG. H—Guinea pig affected with trembles. This animal is unable to control its movements, and general debility is indicated by the drooping ears and partially closed eyes.

PLATE 6.

FIG. I—A pig at the beginning of trembling.

FIG. J—The tremors have become so violent within a few moments that the animal has settled backward upon her haunches and is squealing.

PLATE 7.

FIG. K—A resting posture assumed by falling forward from the position in Fig. J.

FIG. L—The same animal, prostrate. This position may be taken following Fig. K, or the animal may topple over from a standing posture.

PLATE 8.

FIG. M—Acute parenchymatous nephritis. From Lamb No. 244. *a*, tubule in earlier stage of cloudy swelling; *b*, a tubule in advanced stage of cloudy swelling; *c*, an area infiltrated with round cells and polymorphonuclear leucocytes.

PLATE 9.

FIG. N—Glomerulitis and cloudy swelling of Lamb No. 200. *a*, glomerule; *b*, tubules in state of cloudy swelling.

PLATE 10.

FIG. O—Tube casts from urine of Lamb No. 200 (*a*).

FIG. A

FIG. B

FIG. C

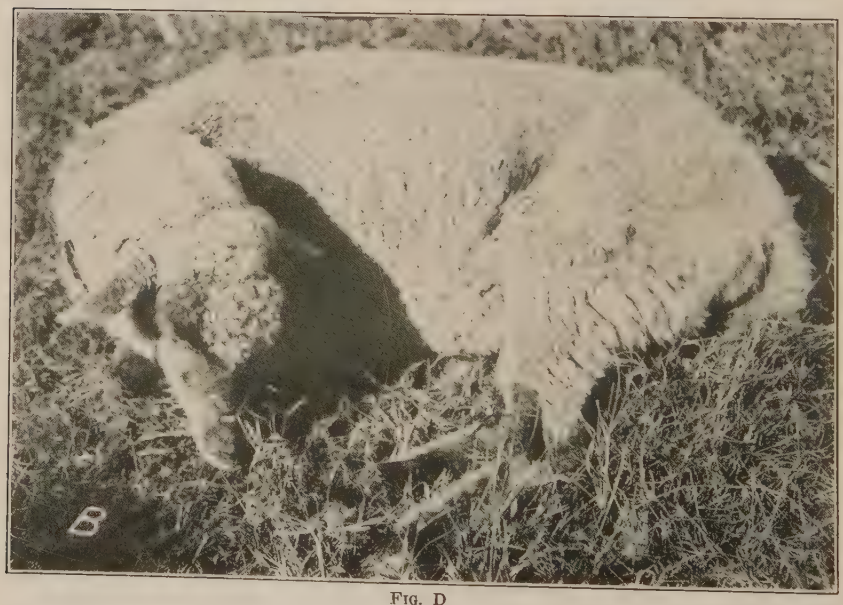

FIG. D

FIG. E

FIG. F

FIG. G

FIG. H

Fig. 1

Fig. 2

FIG. K

FIG. L

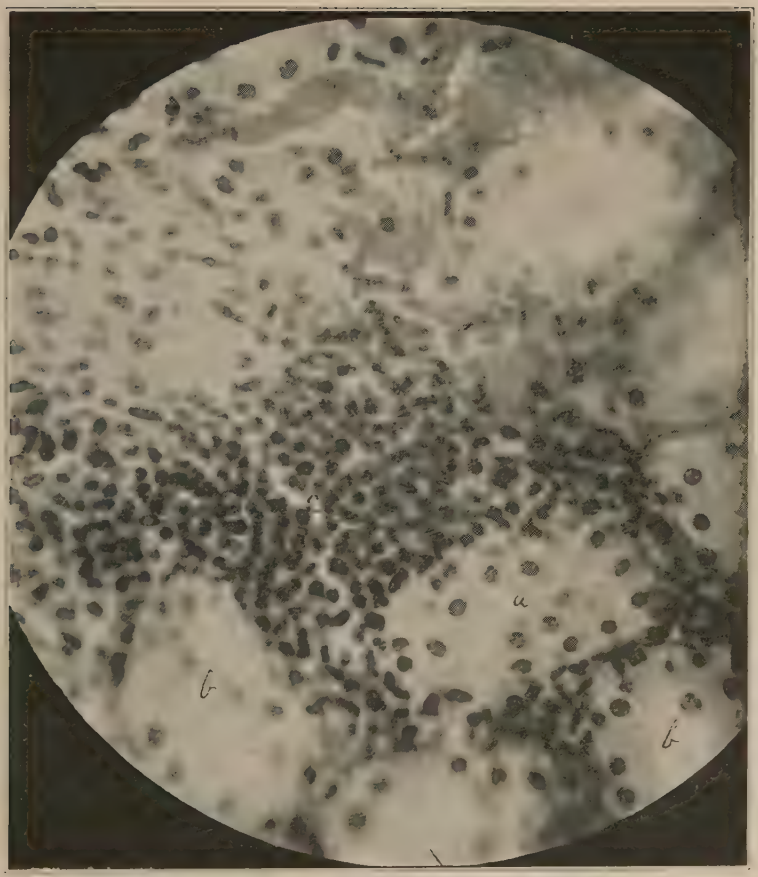

FIG. M

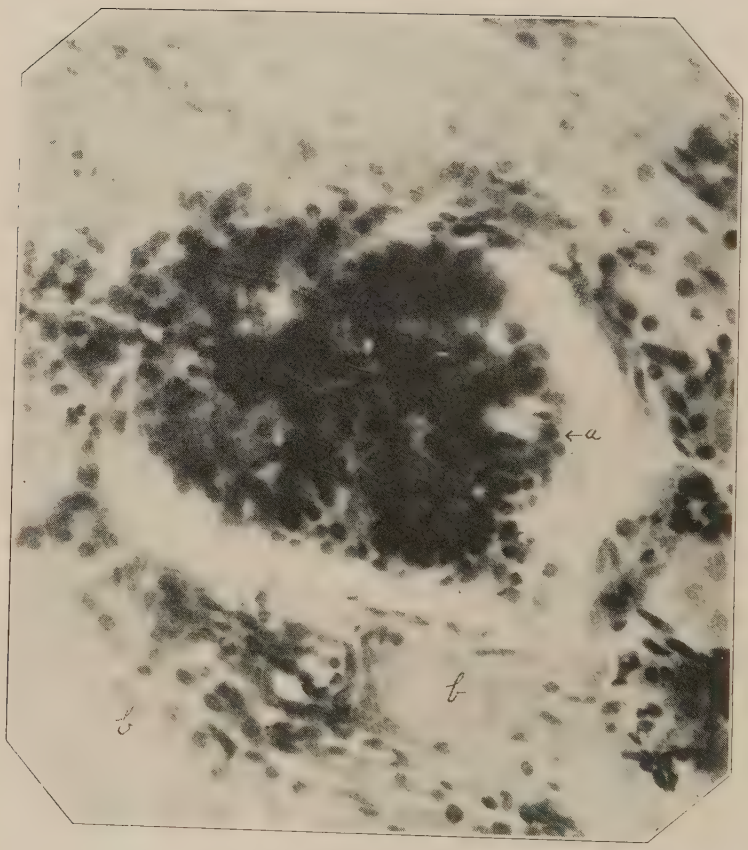

Fig. N

FIG. O